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EPIDEMIOLOGIC AND ETIOLOGIC STUDIES OF ACUTE POLIOMYELITIS IN PENNSYLVANIA*

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READ BY HOWARD T. KARSNER, M.D.
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During 1907 some 200 cases of poliomyelitis developed in a district in the northwestern section of Pennsylvania, extending from 78° 55′ to 80° 15′ west longitude and from 41° to 41° 30′ north latitude. The outbreak apparently began the latter part of July in Elk County and in early August in Venango County, appearing first in Elk County at Ridgway and in Venango County at Oil City; later at Du Bois, in Clearfield County and at Eau Claire in Butler County. In this outbreak the height of the epidemic seemed to be reached the latter part of September and by the end of November the disease was practically stamped out. A small outbreak occurred in Adams County during July and August, 1908. Sporadic cases, only, occurred during 1909.

During the summer of 1910 an epidemic of considerable proportions developed in widely separated sections of the state, reaching a total of 1,076 cases before dying out in the early winter months. The 1910 epidemic began in June in the Lehigh Valley, in July in Lancaster County and in Potter County, and later small outbreaks developed in Westmoreland and Fayette Counties, with scattering cases throughout fifty-five counties. In the Lehigh Valley in the vicinity of the two Bethlehems, Allentown and Catasauqua, the outbreak assumed rather alarming proportions and the same may be said of Lancaster County. In Philadelphia the greatest number of cases occurred in a beautiful section of Germantown, in the northern part of the city, and in a new and rather open section of West Philadelphia, with well paved streets and plenty of shade.

The 1,076 cases reported during the year 1910 were grouped geographically with reference to topography, showing conclusively that elevation played no part, as cases occurred at Philadelphia near sea level

*Read in the Section on Practice of Medicine of the American Medical Association, at the Sixty-Second Annual Session, held at Los Angeles, June, 1911.

in considerable numbers and others were reported in areas fully 2,500 feet above the level of the sea. Similar charting was made with reference to distribution of surface waters, with negative results. The only features of this part of the analysis worthy of mention are that moisture and possibly open water-courses may have played some part in the distribution of the disease.

In classifying cases by geologic formation it seems to hold true that over sand and gravel formation the disease was less prevalent and that it was more prevalent in districts not so favorable for drainage. The character of the surface of the earth in each locality and of the subsoil seems to have been worthy of special note in this relation; and while it is of no distinct value in relation to our present knowledge of the disease, it may be worth recording when making future studies.

We were able to learn nothing of value in relation to the distribution of vegetation other than that the disease was most prevalent after vegetation had reached its height and during the stage when full development of plant life had been reached or passed, the greater number of cases resulting when plant life was on the decline and about the time the harvest season had ended. Possibly fungus growths favored by local death of plants may have furnished a nidus for unusual development of an intermediate host in which the virus may have passed through some stage of its life cycle.

Seasonal distribution shows that the disease is most prevalent during the height of summer and early autumn. This distribution is well shown by grouping reported cases by months of sickening, as follows:

	Cases
January	0
February	3
March	2
April	1
May	4
June	27
July	162
August	336
September	318
October	152
November	52
December	10
Month of onset indefinite in	9

During the 1907 epidemic, the chief of the laboratories spent considerable time in the infected area and secured pathologic materials for laboratory study. Full details of this work will be found in the Department's Annual Report for the year 1907. Research work begun at that time has been continued with slight interruption until the present time. It is doubtful whether monkeys inoculated at that time developed a true polio-

myelitis; probably the virus secured was not fresh enough for research work. Bacteriologic studies made at that time were not productive of results.

With the beginning of the 1910 outbreak a branch laboratory was opened in Bethlehem through the cooperation of St. Luke's Hospital, and later a second branch laboratory was opened in the city of Lancaster through the courtesy of the city chemist. A great mass of data was secured, and a number of autopsies were performed. The tissues, together with a number of lumbar punctures, gave us constant material for laboratory study, and as soon as good strains of virus were secured inoculation experiments gave us the disease in considerable numbers of cases in artificially infected monkeys.

In addition to making careful studies of tissues and spinal fluids secured from the bodies of those suffering from the disease and in making careful inoculation experiments with these materials, a vast amount of work was done in studying smears of blood and of nasal mucus. Careful studies of bowel contents and urine were carried out, an offer being made to the physicians throughout the state to study all such materials forwarded to the laboratory, together with an offer to send them shipping containers. It is very gratifying to report that the laboratory staff in carrying out this work have confirmed the published researches on poliomyelitis and our hopes at one time were greatly encouraged by a rather constant finding of a microorganism which we were unable, until recently, to grow in pure culture, in the blood of children suffering with the disease and in the blood of monkeys suffering from this disease.

Details of these reports were published from the laboratory in March, 1911. At that time we claimed nothing more than that the organism was found with great regularity in the stained blood of human and experimental poliomyelitis. The only thing new to add concerning it at this time is its demonstrated motility. We are continuing work with a series of experiments and continually propagating several strains of virus with the hope that at some time we will learn what its etiologic significance may be.

RESULTS OF INTENSIVE STUDY OF 748 CASES

An intensive study was undertaken by the department, resulting in a more or less complete record of 748 cases, giving details of physical conditions of the premises in which the patient sickened, the history of any possible exposure either to human cases of this disease or to domestic animals that may have had paralysis, the notes being so complete as to include possible exposure to flies, ticks, mosquitos, ants or any biting insect; exposure to heat, cold or dampness; exposure through swimming,

wading or paddling and exposure to dust. A detailed clinical record was secured from the greater number of these cases giving the duration of the fever, the average range of fever, pulse-rate, date of onset of paralysis; full notes as to other cases in the family or neighborhood, a note of the extent of the paralysis at the height of the disease, and finally a note of the extent of residual paralysis existing several months after all symptoms of acute illness had subsided.

We are very greatly indebted to upward of 600 physicians practicing in the commonwealth for all of these detailed records, the compilation of which would not have been possible but for their loyal cooperation.

Detailed epidemiologic records were forwarded by 605 physicians, covering 748 cases.

528	physicians	reported	1 case	each
45	physicians	reported	2 cases	each
17	physicians	reported	3 cases	each
7	physicians	reported	4 cases	each
4	physicians	reported	5 cases	each
1	physician	reported	6 cases	
2	physicians	reported	8 cases	each
1	physician	reported	10 cases	

A few interesting observations may be summarized from the many points developed in this intensive study.

Out of 773 cases of poliomyelitis, fifty-nine gave a distinct history of exposure to previous cases, the sexes being equally divided. Nationality seems to play no particular part in this disease, the vast majority of those contracting poliomyelitis being American-born. Males have more frequently contracted the disease than females. Out of this series of cases 437 were males, and 336 were females. But three of the colored race (two males and one female) sickened. In forty-four instances secondary cases developed in the household.

Other acute illnesses two months prior to the development of infantile paralysis seemed to show but little influence. In three instances whooping-cough existed; in three, intestinal indigestion; in five, measles; in ten, diarrhea; in thirteen, gastro-enteritis; in four, influenza; in nine, tonsillitis; in four, acute enteritis.

Great exposure to heat, cold and dampness was noted in comparatively few instances. Great heat was recorded in sixty-five cases; exposure to cold in twenty-seven; exposure to dampness in eighty-nine.

A total of thirty patients are reported to have met with some minor accident a short time previous to the onset of poliomyelitis.

It was somewhat surprising to find over-exertion reported so seldom, a total of twenty-eight cases being recorded, twenty in the male sex, the exertion often consisting of hard work in the open field.

In nineteen cases a history of automobile riding was noted; in sixteen, swimming; in twenty-nine, wading in open streams; in thirty-seven, pad-

dling in water; in 157 instances the individual contracting the disease constantly ran barefoot.

The prevalence of other diseases in the community during the outbreak of poliomyelitis was not as great as has been reported by some authorities. The diseases of particular moment frequently recorded in infected communities were tonsillitis twenty-five times, gastro-intestinal disturbances forty-seven times.

The date of onset by months is of peculiar interest. Occasional deaths from this disease were recorded during the early months in the year, one in January, two in February and two in April. The disease apparently became more frequent the latter half of June, in each instance in communities where patients had died from the infection at some time during the winter months. In June twenty-four cases were reported; in July 120; in August 262; in September 230; in October 130; in November forty-one; in December ten; a total of 1,076 cases being reported to the department during the twelve months.

By action of the Advisory Board of the State Department of Health, poliomyelitis was made reportable Jan. 7, 1910, general advertisement of the regulation taking place immediately, but individual notices were not mailed to physicians until July, so it is possible that some cases were not reported in the first half of the year. A total of 240 certificates were filed with the department giving poliomyelitis as the cause of death. This mortality shows the disease to have been unusually virulent, even granting that a good many cases may have been missed because it had been so recently made reportable.

The average duration of the fever was about four days. The series of cases studied carefully from the family physicians' notes show that in fourteen cases the fever lasted less than twenty-four hours; in thirty-five, two days; in sixty-eight, three days; in sixty-five, four days; in seventy-two, five days; in thirty-four, six days; in 137, one week and over; in eighty cases, two weeks and over.

The temperature range averaged 99 to 104 + F., the records in twelve cases showing 99 to 100; in fifty-four it was 100 to 101; in 106 cases, 101 to 102; in 147 cases, 102 to 103; in 119 cases, 103 to 104; in sixty-five cases, 104 and over.

The pulse-rate was increased in a large percentage of the cases, the average rate being near 100. In twenty-two instances a record is made of a rate above 150. In a vast majority of the cases the pulse tension is given as high.

In tabulating the symptoms present during the onset and early stage of the illness we find irritability present in 372 cases; stupor in 225; nausea in 343; vomiting in 366; retraction of head in 267; retraction of back in 192; nervous twitchings in 345; convulsions in sixty-one; diar-

rhea in 159; constipation in 349; retention of urine in 118; incontinence of urine in ninety-seven; insomnia in 291; sleepiness in 244, and sore throat in 101 cases. These symptoms seem to apply with great uniformity to both sexes.

Skin eruption was recorded in sixty-three instances. A scarlatiniform erythema was described several times.

It is worthy of note that the presence of pain and tenderness was recorded in 564 cases of the 773 studied intensively. In a very large majority of the cases pain was most severe in the area of the body later showing paralysis and the pain usually subsided on the appearance of paralysis. A greater number of patients complained of pain in the spinal region alone than in any other area of the body, a total of sixty-nine having pain in this region only. Fifty-one complained of spinal and lumbar pain, and in addition, of pain in all extremities. Thirty-three complained of pain in the lumbar region only, nineteen of pain in the cervical region and a total of thirty-seven complained of pain in the large joints, shoulders, hips or elbows; two complained of it in the left thigh only, three in the right thigh, one in the left hand, one in both feet and one in the right foot only. Abdominal pain was not frequent except as associated with nausea and vomiting.

In a few instances (thirty-four) evidence of insect bites was noted. Particulars of these marks will be found in another part of the paper.

In this series of 773 cases, 142 patients (18.4 per cent.) recovered without paralysis and 294 (71.6 per cent.) recovered with considerable residual paralysis.

The distribution of paralysis when at its height presents some interesting features, the following table showing how frequently the extremities alone were involved:

Extremity	Times involved	Extremity	Times involved
Left arm only	16	Both legs only	120
Right arm only	20	Left hemiplegia	35
Left leg only	74	Right hemiplegia	42
Right leg only	69	All four extremities	78
Both arms only	4		

In addition to the seventy-eight instances in which the four extremities were involved, additional parts were paralyzed as follows:

All extremities and both eyes	Once
All extremities, right eye and right face	Once
All extremities, left eye and neck	Once
All extremities, back and abdomen	Once
All extremities, left face, left eye, neck, back and abdomen	Once
All extremities and both eyes	Once
All extremities, neck, back and abdomen	Once
All extremities, neck, back, abdomen and left face	Once

In addition to the 120 cases having both legs only paralyzed, the following cases had additional parts involved:

Both legs and right face	Once
Both legs, right arm and abdomen	Once
Both legs, back and abdomen	Once
Both legs, right face, right eye and right forearm	Once
Both legs and right arm	3 times
Both legs and left arm	Once
Both legs, right arm and right face	Once
Both legs, right arm and neck	Once
Both legs, right arm, right eye and right face	Once

Crossed paralysis was found as follows:

Right upper extremity and left lower extremity	6 times
Left upper extremity and right lower extremity	5 times

In thirty-four instances one or both legs were paralyzed, either alone or in combination with some other part of the body.

In nineteen the right face was paralyzed twice with only the eye or eye and neck involved, and seventeen cases in connection with some other parts of the body.

The left face was involved in twenty-two cases, always in connection with some other part of the body.

Impairment of intelligence was noted in twenty-nine instances.

Housing conditions show that in 149 instances the individual sickened in a large home; in 219 instances in a medium sized home, and in 164 instances in a small dwelling.

When classified with reference to the number of members of the household the tabulation shows two instances in a family of one; thirteen in a family of two; eighty-six in a family of three; 154 in a family of four; 121 in a family of five; ninety-five in a family of six; sixty-two in a family of seven; thirty-three in a family of eight; twenty-three in a family of nine; twenty-three in a family of ten and over.

With reference to the number of children in the household, the tabulation shows 106 instances in which there was one child; 174 in which there were two children; 110 in which there were three children; ninety in which there were four; fifty-nine in which there were five; twenty-two in which there were six; seventeen in which there were seven; twenty in which there were eight; five in which there were nine; four in which there were ten and over; eighteen in which there were none, with 148 unstated cases.

Out of 773 cases contact occurred as follows:

Certain direct contact with acute case	59
Certain direct contact with abortive case	7
Certain direct contact with chronic case	2
Certain direct contact with acute case by second person	5

Adults exposed escaping paralysis.....1,678
Children exposed, escaping paralysis.....1,062
Children sleeping in same bed room with acute case, escaping paralysis.... 261

These figures establish the fact that the danger of transmission from one member of the household to another member of the same household is not great and when we consider the number of instances in which other children slept in the same bed-room with the child contracting poliomyelitis, it seems still more remarkable that so few secondary cases occurred. In 289 instances children slept in the same bed-room, only twenty-four contracting the disease.

In nine instances the disease developed in children after having visited communities where this disease was known to be prevalent. In five cases the possibility of transmission through a second individual seemed probable. These will be given in detail with the case history. In a number of instances suggestive illness occurred in the same household with frank cases of paralysis. A few such cases will be cited with their histories.

Further studies of household conditions showed that in 390 homes doors and windows were screened. In 128 homes sanitary conditions are classified as excellent; in 215 homes as good; in 226 as fair; in sixty-six as bad, with 138 unstated.

Mosquitoes were reported as having access to the house 324 times.

The dwelling stood near a stable or barn in 297 instances; near a poultry house 289 times; near a privy 275 times; and forty-seven times a public garbage dump is reported near the residence. Stagnant water nearby is reported seventy-five times; near open streams in 171 instances; near open drains in 140 instances.

In 410 instances trees are reported in the immediate vicinity of the dwelling; in 122, shrubbery. The particular trees enumerated will be found in a table.

Sanitary plumbing is reported in 277 homes; outside closets in 476.

Household garbage was disposed of to hogs on the premises in thirty-six instances; was burned in thirty-eight; a public system of disposal was reported 231 times; was buried in four instances; thrown on surface of ground 162 times; fed to other domestic animals eleven times.

The water-supply to the household was given as public in 327 instances; well in 194 instances; spring in sixty instances and cistern in thirty-three instances.

The ice-supply was given as natural in eighty-four instances; artificial in 164 instances; none used at all in 322 instances; with 203 unstated.

The milk-supply was given as one cow in 167 instances; breast-fed in twenty-five instances; condensed in five instances; in bottles in 194 instances; in cans in 112 instances; in own receptacles in twenty instances.

Fruits and vegetables used prior to illness in the various households and partaken of by those ill may be well summarized in the following table:

Common varieties	117	Watermelon	2
Cabbage	15	Canteloupe	3
Potatoes	19	Pineapple	1
Lima beans	4	Grapefruit	1
String beans	6	Bananas	51
Peas	10	Oranges	47
Parsnips	1	Peaches	36
Carrots	1	Apples	115
Tomatoes	28	Green apples	1
Corn	8	Plums	20
Parsley	1	Grapes	14
Cucumbers	3	Green grapes	2
Celery	7	Cherries	15
Radishes	9	Berries	21
Onions	17	No vegetables used	116
Lettuce	18	Not stated	55

Fig. 1.—Photomicrograph of pure culture of microorganisms found in the blood of patients with acute anterior poliomyelitis, showing long and short forms of the organism.

Vermin were reported as follows:

	Houses
Flies were present in	383
Mosquitoes were present in	212
Mice (house) were present in	149
Rats were present in	77
Ants were present in	85
Roaches were present in	90
Bedbugs were present in	91
Spiders were present in	127
Mice (field) were present in	43
Biting flies were present in	169
Ticks were present in	14

Trees and shrubbery stood near the infected house as follows:

Trees		Shrubbery	
Fruit	168	Roses	26
Maple	150	Grape Vine	10
Poplar	30	Lilacs	8
Oak	21	Honeysuckle	6
Pine	11	Hedge	3
Willow	9	Vines	1
Locust	9	Snow-balls	1
Chestnut	9	Locust	1
Horse-chestnut	9	Japanese hop vine	1
Elm	4	Cedar	1
Beech	4	Berry	1
Walnut	3	Scrub-apple	1
Linden	2	Maple	1
Cottonwood	2	Mock-orange	1
Cedar	2	Clematis	1
Birch	1	Underbrush	1
Spruce	1	Privet and thorn hedge	1
Shumac	1	Kind not stated	52
Ash	1		
Kind not stated	23		

Data as to Domestic Animals

240 homes had dogs without sickness
264 homes had cats without sickness
254 homes had chickens without sickness
57 homes had birds without sickness
180 homes had horses without sickness
155 homes had cows without sickness
1 home had 1 dog with sickness
3 homes had chickens with sickness (paralysis)
1 home had 1 bird with sickness (paralysis)
1 home had 1 horse with sickness
1 home had 2 cats with sickness

Insect Bites

Mosquito bites appeared in 15 cases as follows:

Back	1	Body	1
Hands	3	Thighs	1
Face	4	Chest	1
Neck	3	Location not stated	1

Bedbug bites appeared in 2 cases as follows:

Thighs	1	Chest	1

Unknown insect bites appeared in 17 instances as follows:

Face	4	Thighs	2
Neck	2	Temporal region	1
Body	4	Location not stated	3
Head	1		

In many histories rats were reported on the premises. Field mice were frequently found. In 149 homes house mice were prevalent; in 383 homes ordinary flies were found; biting flies were reported 169 times; bedbugs ninety-one times; roaches ninety times; ticks fourteen times; ants eighty-five and spiders 127. Mosquitoes were noted in 212 instances.

Unusual insects were reported in eighteen instances, particulars being found elsewhere.

In three instances paralytic disease occurred in animals, the particulars being set forth elsewhere.

The underclothing worn by those sickening is reported as being cotton in 304 cases; woolen in eighty-two; half cotton and half wool in ten. The stockings were reported as being cotton in 300; woolen in seventy-eight; half cotton and half wool in six.

Several centers of unusual prevalence were noted, one in the vicinity of Galeton near the line between Potter and Tioga Counties, at a great elevation in the northern part of the state; one in the vicinity of the Bethlehems and Allentown in Northampton and Lehigh Counties in the east central section of the state; one in Lancaster County in the city of Lancaster and adjacent rural districts in the south central part of the state and one each in Luzerne and Westmoreland Counties in the southwestern section of the commonwealth, and in Philadelphia county in the section of the city known as Germantown and in a part of West Philadelphia west of the Schuylkill River. The disease was found, however, in fifty-eight counties out of sixty-seven. Grouped by counties the following table shows the distribution throughout the state:

TABLE 3.—SHOWING DISTRIBUTION OF CASES AND POPULATION

County	Cases	Population	County	Cases	Population
Adams	0	34,319	Lancaster	150	167,029
Allegheny	89	1,018,463	Lawrence	4	70,032
Armstrong	7	67,880	Lebanon	3	59,565
Beaver	17	78,353	Lehigh	101	118,832
Bedford	1	38,879	Luzerne	15	343,186
Berks	26	183,222	Lycoming	4	80,813
Blair	0	108,858	McKean	15	47,868
Bradford	4	54,526	Mercer	2	77,699
Bucks	27	76,530	Mifflin	4	27,785
Butler	14	72,689	Monroe	6	22,941
Cambria	3	166,131	Montgomery	33	159,590
Cameron	2	7,644	Montour	1	14,868
Carbon	10	52,846	Northampton	140	127,667
Centre	4	43,424	Northumberland	7	111,420
Chester	11	109,213	Perry	5	24,136
Clarion	0	36,638	Pike	1	8,033
Clearfield	1	93,768	Potter	9	29,729
Clinton	0	31,545	Schuylkill	15	207,894
Columbia	7	48,467	Snyder	1	16,800
Crawford	1	61,565	Somerset	7	67,717
Cumberland	4	54,479	Sullivan	0	11,293
Dauphin	11	136,153	Susquehanna	0	37,746
Delaware	16	117,906	Tioga	19	42,829
Elk	2	35,871	Union	1	16,249
Erie	8	115,517	Venango	4	56,359
Fayette	19	167,449	Warren	1	39,592
Forest	0	9,435	Washington	21	143,680
Franklin	6	59,775	Wayne	3	29,236
Fulton	0	9,703	Westmoreland	50	231,304
Greene	1	28,882	Wyoming	2	15,509
Huntingdon	1	38,304	York	6	136,405
Indiana	5	66,210	Philadelphia	143	1,549,008
Jefferson	2	63,090			
Juniata	0	15,013		1076	
Lackawanna	4	259,570			

Adults exposed escaping paralysis	1,678
Children exposed, escaping paralysis	1,062
Children sleeping in same bed room with acute case, escaping paralysis	261

These figures establish the fact that the danger of transmission from one member of the household to another member of the same household is not great and when we consider the number of instances in which other children slept in the same bed-room with the child contracting poliomyelitis, it seems still more remarkable that so few secondary cases occurred. In 289 instances children slept in the same bed-room, only twenty-four contracting the disease.

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TABLE 1.—POLIOMYELITIS GROUPED BY AGE PERIODS

	Cases		Cases
1 month	2	4 to 5 years	58
2 months	1	5 to 6 years	44
3 months	4	6 to 7 years	50
4 months	4	7 to 8 years	24
5 months	7	8 to 9 years	22
6 months	9	9 to 10 years	20
7 months	12	10 to 15 years	45
8 months	7	15 to 20 years	23
9 months	20	20 to 25 years	18
10 months	7	25 to 30 years	8
11 months	8	30 years and over	8
1 to 2 years	346	Not stated	34
2 to 3 years	187		
3 to 4 years	108	Total	1076

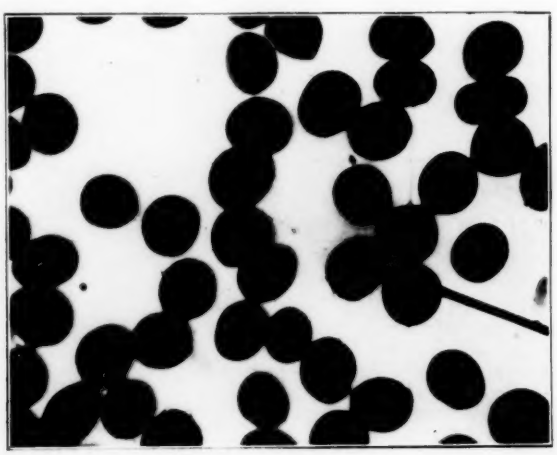


Fig. 2.—Photomicrograph of blood of patient ill of acute anterior poliomyelitis, showing a single organism with bulbous ends connected by a long thin body, attached at one end to red corpuscle in exact center of photograph.

TABLE 2.—DAY OF ONSET OF PARALYSIS

	Cases		Cases
Same day	111	10 days	8
1 day	83	11 days	4
2 days	88	12 days	2
3 days	93	13 days	0
4 days	51	14 days	3
5 days	37	15 days	2
6 days	22	19 days	1
7 days	22	20 days	1
8 days	9	21 days	5
9 days	5	Not stated	126

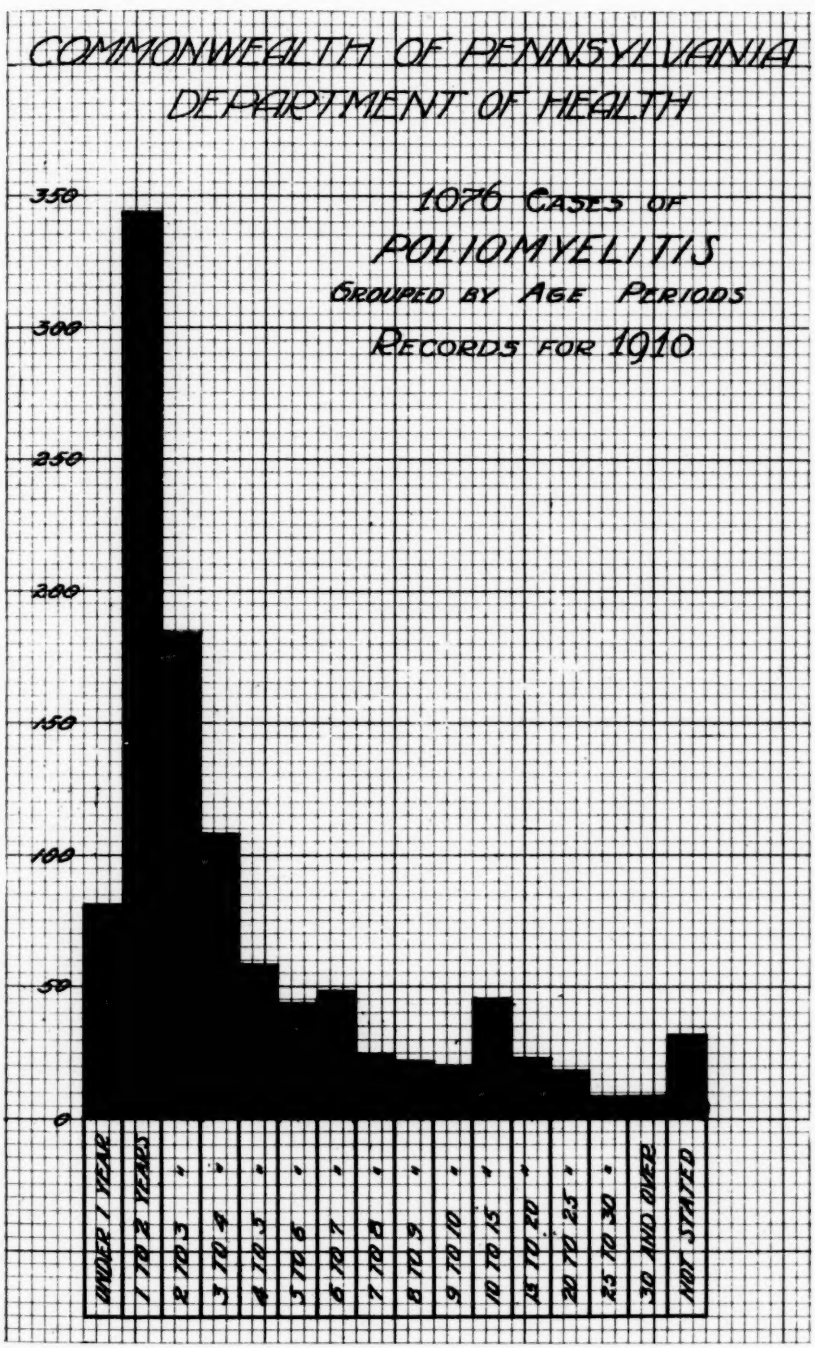


Fig. 3.—Chart showing graphically the cases of poliomyelitis recorded in 1910, grouped by age periods.

Trees and shrubbery stood near the infected house as follows:

Trees		Shrubbery	
Fruit	168	Roses	26
Maple	150	Grape Vine	10
Poplar	30	Lilacs	8
Oak	21	Honeysuckle	6
Pine	11	Hedge	3
Willow	9	Vines	1
Locust	9	Snow-balls	1
Chestnut	9	Locust	1
Horse-chestnut	9	Japanese hop vine	1
Elm	4	Cedar	1
Beech	4	Berry	1
Walnut	3	Scrub-apple	1
Linden	2	Maple	1
Cottonwood	2	Mock-orange	1
Cedar	2	Clematis	1
Birch	1	Underbrush	1
Spruce	1	Privet and thorn hedge	1
Shumac	1	Kind not stated	52
Ash	1		
Kind not stated	23		

Data as to Domestic Animals

240 homes had dogs without sickness
264 homes had cats without sickness
254 homes had chickens without sickness
57 homes had birds without sickness
180 homes had horses without sickness
155 homes had cows without sickness
1 home had 1 dog with sickness
3 homes had chickens with sickness (paralysis)
1 home had 1 bird with sickness (paralysis)
1 home had 1 horse with sickness
1 home had 2 cats with sickness

Insect Bites

Mosquito bites appeared in 15 cases as follows:

Back	1	Body	1
Hands	3	Thighs	1
Face	4	Chest	1
Neck	3	Location not stated	1

Bedbug bites appeared in 2 cases as follows:

Thighs	1	Chest	1

Unknown insect bites appeared in 17 instances as follows:

Face	4	Thighs	2
Neck	2	Temporal region	1
Body	4	Location not stated	3
Head	1		

In many histories rats were reported on the premises. Field mice were frequently found. In 149 homes house mice were prevalent; in 383 homes ordinary flies were found; biting flies were reported 169 times; bedbugs ninety-one times; roaches ninety times; ticks fourteen times; ants eighty-five and spiders 127. Mosquitoes were noted in 212 instances.

Unusual insects were reported in eighteen instances, particulars being found elsewhere.

In three instances paralytic disease occurred in animals, the particulars being set forth elsewhere.

The underclothing worn by those sickening is reported as being cotton in 304 cases; woolen in eighty-two; half cotton and half wool in ten. The stockings were reported as being cotton in 300; woolen in seventy-eight; half cotton and half wool in six.

Several centers of unusual prevalence were noted, one in the vicinity of Galeton near the line between Potter and Tioga Counties, at a great elevation in the northern part of the state; one in the vicinity of the Bethlehems and Allentown in Northampton and Lehigh Counties in the east central section of the state; one in Lancaster County in the city of Lancaster and adjacent rural districts in the south central part of the state and one each in Luzerne and Westmoreland Counties in the southwestern section of the commonwealth, and in Philadelphia county in the section of the city known as Germantown and in a part of West Philadelphia west of the Schuylkill River. The disease was found, however, in fifty-eight counties out of sixty-seven. Grouped by counties the following table shows the distribution throughout the state:

TABLE 3.—SHOWING DISTRIBUTION OF CASES AND POPULATION

County	Cases	Population	County	Cases	Population
Adams	0	34,319	Lancaster	150	167,029
Allegheny	89	1,018,463	Lawrence	4	70,032
Armstrong	7	67,880	Lebanon	3	59,565
Beaver	17	78,353	Lehigh	101	118,832
Bedford	1	38,879	Luzerne	15	343,186
Berks	26	183,222	Lycoming	4	80,813
Blair	0	108,858	McKean	15	47,868
Bradford	4	54,526	Mercer	2	77,699
Bucks	27	76,530	Mifflin	4	27,785
Butler	14	72,689	Monroe	6	22,941
Cambria	3	166,131	Montgomery	33	159,590
Cameron	2	7,644	Montour	1	14,868
Carbon	10	52,846	Northampton	140	127,667
Centre	4	43,424	Northumberland	7	111,420
Chester	11	109,213	Perry	5	24,136
Clarion	0	36,638	Pike	1	8,033
Clearfield	1	93,768	Potter	9	29,729
Clinton	0	31,545	Schuylkill	15	207,894
Columbia	7	48,467	Snyder	1	16,800
Crawford	1	61,565	Somerset	7	67,717
Cumberland	4	54,479	Sullivan	0	11,293
Dauphin	11	136,153	Susquehanna	0	37,746
Delaware	16	117,906	Tioga	19	42,829
Elk	2	35,871	Union	1	16,249
Erie	8	115,517	Venango	4	56,359
Fayette	19	167,449	Warren	1	39,592
Forest	0	9,435	Washington	21	143,680
Franklin	6	59,775	Wayne	3	29,236
Fulton	0	9,703	Westmoreland	50	231,304
Greene	1	28,882	Wyoming	2	15,509
Huntingdon	1	38,304	York	6	136,405
Indiana	5	66,210	Philadelphia	143	1,549,008
Jefferson	2	63,090			
Juniata	0	15,013		1076	
Lackawanna	4	259,570			

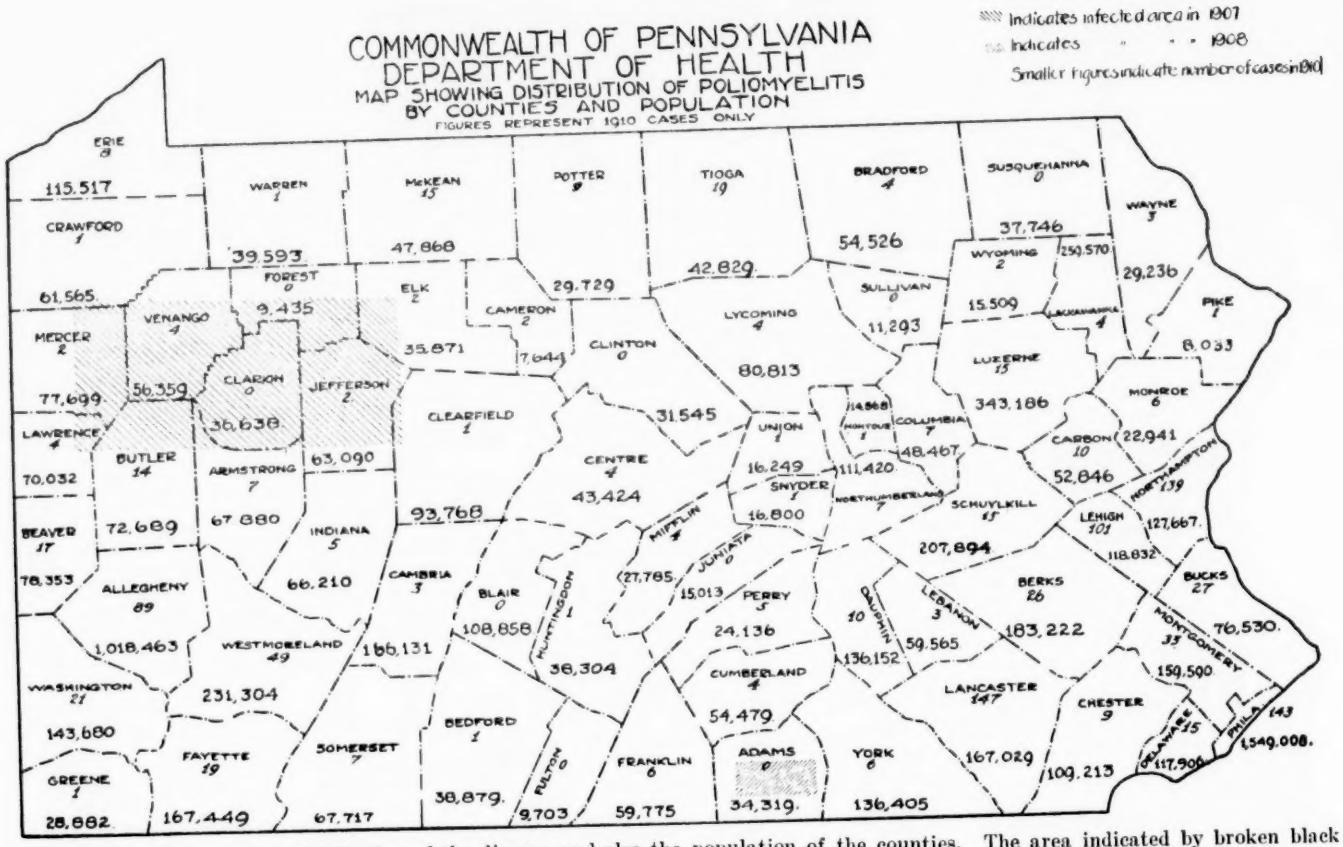


Fig. 4.—Map showing distribution of the disease, and also the population of the counties. The area indicated by broken black lines shows the district in northwestern Pennsylvania affected in 1907 and the district in Adams county affected in 1908.

It is interesting to note that few cases developed in Elk, Venango and Clearfield Counties, where epidemics were reported in 1907, and in Adams County, where a small outbreak occurred in 1908. The exception, however, occurred in Butler County, where a few cases developed in 1907, and fourteen cases in 1910.

The laboratory staff, working from the branches opened in the field, made an intensive study of seventy-three cases during life and a study of pathologic materials from eleven fatal cases, doing a great deal of routine work resulting in statistics too elaborate to refer to more than incidentally in this paper. A composite table of blood-counts alone, when grouped by day of disease on which count was made, is worthy of reproduction.

Day	Polynuclears	Small Lymphocytes	Large Lymphocytes	Eosinophils
2nd to 5th	52.2	34.2	10.1	3.5
6th to 9th	47.2	34.6	13.2	5.
After 10th	51.4	32.8	13.1	2.7

Ordinary leukocyte counts were made in a series of cases. The results seem to show a high degree of leukocytosis up to the ninth day of illness. Spinal fluids were studied eleven times, in each instance fluid being secured during the active stage of the disease. Neutral broth cultures showed the common diplococcus in every such fluid, but in no instance were we able to secure paralysis by inoculation with this organism.

A very large number of swabbings from the nasopharynx were secured and from fourteen such swabbings attempts were made to inoculate five monkeys by applying the centrifugal sediment resulting from macerating these materials in salt solution, swabbing the sediment over the mucous membranes and as nearly as possible placing sediment over the cribriform ethmoidal plate. All of these results were negative.

Six monkeys and seven rabbits injected under the skin with this material gave negative results. These findings seem to show that there is not great danger from the discharges, even though we do succeed in producing the disease by using the actual mucous membranes in the nasopharyngeal area.

Inoculation experiments made in an attempt to produce immunity in monkeys was to a very high degree successful. Attempts to give the disease to rabbits was only in part successful, as we failed absolutely in our attempts to transmit the disease from the rabbit developing paralysis to other rabbits or back to monkeys. It is possible that failure in this experiment occurred because the paralysis in the rabbit was not demonstrable until two weeks after inoculation.

In several communities an unusual number of yellow butterflies were reported. A series of these butterflies were collected, killed and macer-

TABLE 4.—SHOWING DETAILS OF CONTACT CASES

No.	Name	Contact	Manner	Same House	Date of Contact	Onset of Paralysis
160	J. Z.	From Trenton, N. J., direct contact in Lancaster on July 19. Indirect contact through father July 20	Direct and Indirect	No	July 19-20	July 20
20	H. H.	E. V. Philadelphia	Direct	No	3 yrs. or less	July 1
733	L. H.	D. F.	Direct	No	July 14	July 23
315	C. S.	N. D.	Direct	No	Aug. 24	Sept. 1
188	J. C. S.	H. G., New Brighton	Direct	No	Aug. 21	Sept. 1
1	M. M.	M. M.	Direct	No	July 27	Aug. 10
34	C. D.	K. L.	Direct	No	Aug. 26	Sept. 9
17	M. C.	[illegible] T.	Direct	No	July 10	Aug. 24
715	A. E.	G. E.	Direct	Yes	Sept. 1	Sept. 10
499	F. O.	Case in same house	Direct	Yes	Aug. 5	Aug. 25
319	W. R.	Brother	Direct	Yes	Unstated	Aug. 9
577	C. H.	Brother	Direct	Yes	Aug. 25	Sept. 3
296	J. N.	Several cases in Scranton	Direct	No	July 3	July 10
492	W. G.	1619 Chew St.	Direct	No	July 10	July 12
501	J. K.	Neighbor	Direct	No	July 12	July 26
255	B. W.	S. H.	Direct	No	Aug. 18	Aug. 25
390	L. E. L.	Child. Smock, R. F. D.	Direct	No	Oct. 19	Nov. 2
670	J. S.	Philadelphia (L. children)	Direct	No	June 21	July 1
700	N. Y.	A. Y.	Direct	Yes	Constant	Sept. 27
704	W. Y.	A. Y.	Direct	Yes	Constant	Sept. 30
691	F. C.	E. F.	Direct	Yes	Constant	Aug. 7
696	S. B.	K. B.	Direct	Yes	Oct. 8	Oct. 11
693	H. R.	H. R., N. Bethlehem	Direct	Unstated	June 20	July 7
847	F. S.	Other case in family	Direct	Yes	Unstated	July 25
846	R. S.	F. S.	Direct	Yes	July 25	July 29
446	M. U.	J. C. (Slept in same bed) No. 527	Direct	No	June 15	June 26
261	M. H.	W. H.	Direct	Yes	July 24	Aug. 1
268	L. M.	Case 1067	Direct	Yes	Constant	Aug. 15
239	G. C.	K. C.	Direct	Yes	Constant	Sept. 11
610	L. H.	N. H.	Direct	Yes	Aug. 17	Aug. 24

268	L. M.	Case 1067	Direct	Yes	Constant	Sept.
239	G. C.	K. C.				

610	L. H.	N. H.	Direct	Yes	Aug. 17	Aug. 24
94	A. R.	M. R.	Direct	Yes	Oct. 31	Nov. 4
234	M. O.	C. O. (Case 554)	Direct	Yes	Constant	Sept. 3
329	F. O.	C. O. (Case 554)	Direct	Yes	Constant from 8/23	Sept. 2
342	M. W.	R. W. (Case 338)	Direct	Yes	Constant	Sept. 19
666	W. A.	Brother (Case 665)	Direct	Yes	Aug. 24	Sept. 8
602	M. H.	Brothers and sisters	Direct	Yes	Aug. 1	Aug. 7-8
585	C. E.	Sister	Direct	Yes	Aug. 1	Aug. 8
434	D. G.	Child from Huttles, Pa.	Direct	Yes	July 15	Aug. 11
743	H. W.	While waitress served a baby short time before who died from disease	Direct	No	Unstated	Oct. 5
1040	P. S.	Brother	Direct	Yes	Aug. 2	Aug. 9
2	M. M.	Visit of mother to other case	Indirect	No	Sept. 24	Oct. 13
393	P. C.	Grandmother from Lancaster ten days prior former contact with case	Indirect	No	Sept. 21	Oct. 1
606	— D.	Mother ironed Huber family wash. Case 602	Indirect	No	Aug. 1-8 inc.	Aug. 12
269	B. T.	Cases in neighborhood	Indirect	No	Unstated	Sept. 15
231	A. H.	Cases within a mile	Indirect	No	Unstated	Aug. 1
201	N. K.	Came from Trenton week previous to June 5	Indirect	No	Unstated	July 7
27	D. A.	Other case in neighborhood	Indirect	No	Unstated	Aug. 5
234	N. H.	Visited Lancaster Co.	Indirect	No	Sept. 25	Oct. 1
109	A. S.	Colerain Twp. Lancaster Co.	Indirect	No	About Aug. 1	Aug. 18
304	J. D.	In Pottstown prior to Sept. 24. In Elizabeth from Sept. 24 to 26	Indirect	No	Prior to Sept. 26	Oct. 1
657	J. C.	Allentown on or about Sept. 20	Indirect	No	Unstated	Oct. 1
325	C. W.	B. family	Indirect	No	Unstated	Sept. 20
357	F. T.	R. M. milk from M. cow	Indirect	No	Constant and Unstated	Oct. 14
385	E. Y.	M. case	Indirect	No	Unstated	Nov. 4
184	M. B.	Philadelphia	Indirect	No	Unknown	Aug. 8
363	B. S.	J. S. Brookville, R. D.	Unstated	No	Aug. 1	Dec. 1
403	M. B.	S. V. Snedekerville, Pa.	Unstated	No	Sept.	Oct. 1

ated. Inoculation experiments from the resulting material failed uniformly to produce paralysis.

In the Bethlehems a blight among Norway maple trees attracted considerable attention and it was thought by many citizens that this disease was more prevalent near houses where cases of poliomyelitis existed. A careful examination of these conditions showed that the blight was not confined to the Norway maple and that there was no greater involvement of trees in the vicinity of the affected houses than elsewhere. Examination of the blighted branches showed a delicate mycelium running through the mesophyl of the leaves that was not identical with the oidium of Westphalia. The study of this mycelium gave us negative results. A large number of specimens of blood smears, samples of feces, urine and nose and throat swabbings were sent us by practitioners, but aside from finding microorganisms in the blood with great uniformity, nothing worthy of note was seen.

EXTRACT FROM LABORATORY REPORT PUBLISHED MARCH 2, 1911

In examining the blood from acute cases of poliomyelitis in human beings, and also in monkeys in which the disease was produced experimentally, an organism was found, different in morphologic characteristics from any heretofore described which may or may not, on further investigation, prove to be the etiologic factor in the causation of the disease. Blood smears being fixed in methyl alcohol for one minute and stained with carbol-thionin, the organism appears as a faintly-stained blue rod with regular cell wall about 10 microns long and about 8 microns in width, curved at an angle of 60 to 75 degrees at one end, occasionally at both ends. At times, the curved end is bulbous. Some of the organisms appear to have a very finely granular protoplasm when the highest amplification is employed. They may be discerned by means of a 4 mm. dry objective but their characteristics are much more satisfactorily delineated under the 1/12 oil-immersion lens. They are found free in the serum as well as within the body of the red blood-cell.

The organisms do not retain the violet color when stained by the method of Gram but assume the color of the counter stain which, as generally used in this laboratory, is a very dilute solution of carbol-fuchsin.

The bloods examined were from ten different cases of acute poliomyelitis in children and were taken during the epidemic of last summer and autumn, and from thirteen cases of the disease during the acute stage, which had been produced experimentally in as many monkeys.

Blood smears from three normal human beings were carefully examined and although the search for these organisms was diligently made, none was found. Smears were made from the bloods of thirteen normal monkeys with negative results. After inoculation with the virus these same monkeys gave positive results. The blood of other normal monkeys gave negative results.

Blood smears were stained with iodin and sulphuric acid in order to test the organisms for cellulose, but no blue stained organisms were seen.

Smears from the cords and brains of paralyzed monkeys, and from one human case were examined, but none of the new organisms was found.

Filtered virus stained with carbol-thionin and by Gram's method showed none of these organisms.

Defibrinated blood, three weeks to two months old, from two paralyzed monkeys, showed the forms in increased numbers.

Cultures made from the blood of a paralyzed monkey, in blood bouillon, plain bouillon, and blood-agar, examined after having been inoculated three weeks,

showed the presence of the organism in increased numbers. Dorsett's egg medium was inoculated with the same blood at the same time but the organism was not found in smears from the surface of the medium or from the water of condensation.

SUBSEQUENT FINDINGS

Since publishing the above preliminary report on the finding of rod-shaped microorganisms in specimens of stained blood taken from human beings suffering from poliomyelitis and from monkeys in which the disease had been produced experimentally, these microorganisms have been found moving freely in the serum or attached to the side of a red blood-corpuscle in fresh blood taken from three monkeys ill of poliomyelitis. The monkey blood was examined at the time of inoculation and at twenty-four-hour periods up to 168 hours after inoculation. In the blood examined at the time of inoculation and at the twenty-four-hour period no organisms were found. At the end of forty-eight hours, however, a few of the moving microorganisms were found. Their numbers in the fresh blood specimens were increased up to 120 hours, after which time they seemed to appear in about the same numbers till examination at regular intervals was discontinued. At the end of three weeks the motile organisms could still be found in large numbers in the fresh blood.

Examination of the blood of a normal monkey examined at the same period as a control, failed to reveal any of the microorganisms.

The motility was of a slow, sinuous type resembling that of a spirillum. The bulbous ends were readily discernible. At times the organism appeared as standing on end, presenting the bulb uppermost, so that it resembled a large coccus in the microscopic field. Presently it would right itself and the long curved rod terminating in this bulb could be distinctly followed.

Pure cultures of this organism were isolated from the bloods of these three monkeys, on a medium made of the central nervous system of a monkey, combined with agar-agar. After a generation or two on this central-nervous-system-agar, the organism grows well on the ordinary laboratory media.

CHARACTERS OF THE ORGANISM

The morphologic, biologic and biochemic characters of the organism grown on artificial media are as follows:

The best stain to bring out the morphology is carbol-thionin, though Loeffler's alkaline methylene-blue, Giemsa, Wright's, Ziehl-Nielson, carbol-fuchsin and Gram's method demonstrate the organism with no difficulty whatsoever. Stained with carbol-thionin the organism appears as a granulated rod, the young forms measuring 0.6 to 0.8 microns in width by 1 to 2 microns in length. The older forms may appear as long as 10 or 12 microns with a width of 0.6 to 0.8 microns. Many of the indeterminate forms appear as spirals with from two to four loose

turns. The longer forms have in many instances bulbous ends which have somewhat the appearance of spores, though free spores have never been observed.

The organism is actively motile, having a single polar flagellum at one pole only. It has no demonstrable capsule, and it is decolorized by the method of Gram. Colonies on agar are circular, moist, convex, entire, 1 to 3 mm. in diameter. In color they are bluish gray by direct light, old colonies having a yellowish tinge by transmitted light. Their peripheries are translucent while their centers are thickened and appear yellowish-white. Microscopically they are brownish-white, with a finely granular translucent periphery, and an opaque, brown, grumous center.

Agar Slant: Bluish gray with a suggestion of greenish tinge in cultures three or four days old, moist, raised, regular edges, growth along whole length of streak. White beaded growth in stab.

Gelatin: White, beaded growth along needle track with nail-head, moist growth on surface. No liquefaction.

Potato: Moist, cream to brown, abundant.

Central-Nervous-System-Agar: Gray, moist, very abundant along entire path of inoculation.

Egg Medium (consisting of yolk only): Moist, very abundant, spreading, pinkish growth.

Bouillon: Very turbid, white flocculent sediment. In 120 hours a white ring around the glass tube at the level of the surface of the medium.

Litmus Milk: An initial acidity followed by a gradually increasing alkalinity, with a beginning reduction of the litmus at the bottom of the tube. No coagulation of the casein occurs. In four weeks acidification again takes place; reduction of litmus and firm coagulation after five weeks.

There is a slight production of acid in dextrose-agar and saccharose-agar, but not in mannite, maltose or lactose. Gas production does not occur in any of the sugars above mentioned. Mannite turns green after three weeks. The organism grows best in neutral medium, next best in acid, and poorest in alkaline.

Indol is not produced. It seems to grow most abundantly on media rich in phosphates. It does not grow well on media containing much glycerin. The organism grows in the absence of air as well as when the air is given free access.

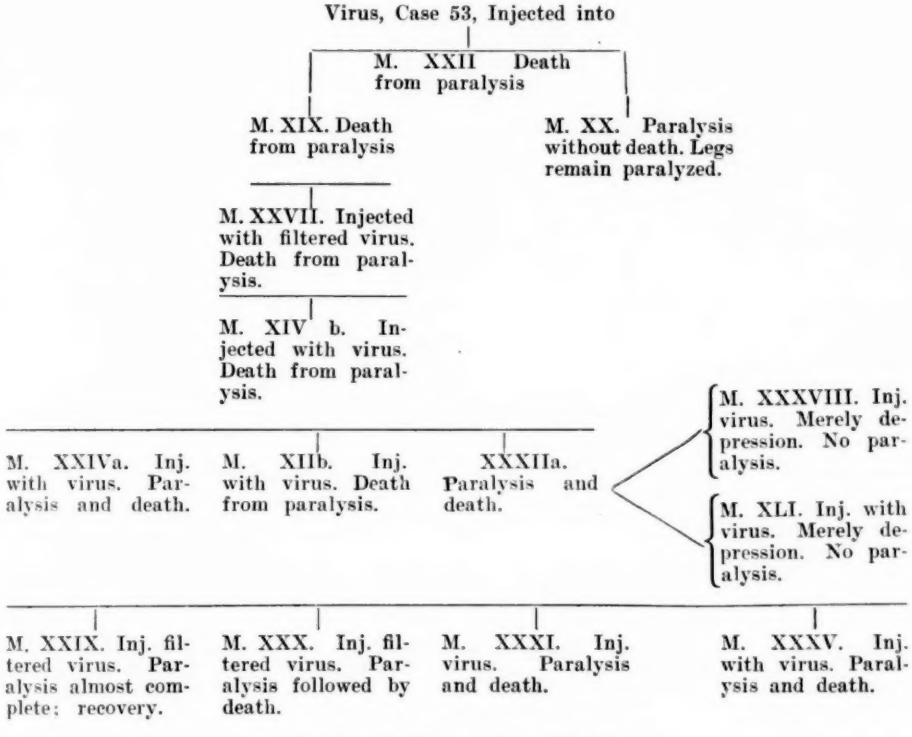
EXPERIMENTAL PRODUCTION AND PREVENTION OF THE DISEASE

Experiments on the production of poliomyelitis in monkeys by using this organism are in progress.

We have published in connection with our laboratory work negative experiments resulting from a good many observations made with great care. On finding virus negative after an autopsy had been performed on a child dead with this disease, we conducted experiments to determine what agent in the embalming fluid might have been destructive, and.

determining that formaldehyd and arsenic were both used in these fluids, a series of experiments were carried out with each, as well as with the fluid itself, solutions being injected at varying intervals as inoculation

TABLE 5.—SHOWING TRANSMISSIBILITY FROM HUMAN CASE TO MONKEY AND FROM MONKEY TO MONKEY


Virus, Case 53, Injected into
M. XXII Death from paralysis
M. XIX. Death from paralysis
M. XX. Paralysis without death. Legs remain paralyzed.
M. XXVII. Injected with filtered virus. Death from paralysis.
M. XIV b. Injected with virus. Death from paralysis.
M. XXIVa. Inj. with virus. Paralysis and death.
M. XIIb. Inj. with virus. Death from paralysis.
XXXIIa. Paralysis and death.
M. XXXVIII. Inj. virus. Merely depression. No paralysis.
M. XLI. Inj. with virus. Merely depression. No paralysis.
M. XXIX. Inj. filtered virus. Paralysis almost complete; recovery.
M. XXX. Inj. filtered virus. Paralysis followed by death.
M. XXXI. Inj. virus. Paralysis and death.
M. XXXV. Inj. with virus. Paralysis and death.

Filtrate of cords of human Case 53
Combined with Monkeys XXX, XXXII, XXXVIII, XLI and XXXV

M. XLIV. Paralysis and death.

M. XLVI. Inj. with virus. Paralysis and death.

M. XLIX. Inj. with filtered virus. Paralysis and death.

experiments to determine whether or not it would be possible to prevent the development of the disease by administration of these chemicals. The results in each instance were negative. Salvarsan was tried in a

series of experiments in order that we might have data concerning the most potent arsenical preparation. These experiments, too, were negative, although they led to the incidental discovery of a positive Wassermann reaction in a monkey.

Abstract Case No. 256 (Laboratory Case No. 53).—G. T., female, aged 7; physician, Dr. George E. Day, Strasburg. Child well to August 23; August 24, stiffness of knee, pain in neck, fever, constipation, dizziness, temperature 102.5 F., no paralysis; August 26, paralysis right leg, both arms, loss of reflex, sensation normal; August 27, worse, pulse rapid, pressure symptoms; lumbar puncture secured 32 c.c. spinal fluid under excess pressure; August 28, slight improvement; 29th, breathing labored, 30th, death 9:00 a. m.; complete autopsy 11:00 a. m. Abundant material for laboratory study was obtained and true pathologic picture found. Tissues gave Noguchi butyric reaction. Emulsion from lumbar cord, bulb, pons, lymph-nodes, cultures from cerebrum, cerebellum, pons, bulb, lumbar cord, lymph-nodes; Gram positive coccus found in cultures taken at autopsy from brain and cord; nothing further by dark-field illumination. Monkeys inoculated with this coccus remained well. Two monkeys received emulsion from cord, pons and bulb into brain; both contracted disease and from this strain of virus successful transmission experiments were secured as illustrated on protocol of transmissibility.

I am greatly indebted to Dr. B. Franklin Royer, Chief Medical Inspector, and the staff of the Division of Medical Inspection, for the compilation of the statistics in this report, and to Drs. Herbert Fox, and J. B. Rucker, Jr., of the Laboratory Division, for the notes of the experimental work carried out under my direction.

RELATIONSHIP OF GASTRIC TO PANCREATIC FAT DIGESTION IN INFANTS *

J. P. SEDGWICK, M.D., AND F. W. SCHLUTZ, M.D.
MINNEAPOLIS

The presence of a ferment in the adult stomach, which has the power of splitting neutral fat into its component fatty acids and glycerin, the gastric lipase, has been confirmed by recent studies.

Although Marcet,[1] Cash,[2] Ogata[3] and Vaughan Harley[4] found fatty acids in the stomach contents, it remained for Volhard[5] to demonstrate the presence of fat-splitting ferment and bring the subject forward for study. Stade,[6] one of Volhard's pupils, confirmed his results and suggested the technic of examination which goes by his name.

Inouye[7] failed to find evidence of a gastric lipase, but Falloise[8] confirmed its presence, and Laquer found the secretion from a Pawlow small stomach to be active in splitting fat, thus proving that the activity cannot be due to regurgitated pancreatic steapsin. Stef. v. Pesthy[9] confirmed the fact that fat is split in the stomach.

The study of the gastric lipase in the infant was first taken up in 1905 and its presence demonstrated by one of us (Sedgwick)[10] and the results published in 1906. This work showed that there is a fat-splitting ferment present in the infant's stomach, and in the glycerin extract of the gastric mucous membrane. It was demonstrated that lipase is present during the first few hours of life in the rabbit, and at least as early as on the fourteenth day in the infant. The fat was found to

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*Read in the Section on Diseases of Children of the American Medical Association, at the sixty-second annual session, held at Los Angeles, June, 1911.

*From the Laboratory of Physiological Chemistry, University of Minnesota.

1. Marcet: Med. Times and Gaz., New Series, 1858, xvii.

2. Cash: Ueber den Anteil des Magens und des Pankreas an der Verdauung der Fette, Arch. f. Anat. u. Physiol., 1880, 323.—Cited from v. Noorden's Handbuch der Pathologie des Stoffwechsels, i, 37.

3. Ogata: Die Zerlegung neutraler Fette in lebendigen Magen, Arch. f. Anat. u. Physiol., 1881, vi, 515; cited from Jahrb. d. Fortschr. d. Thierchemie, 1882, xi, 290.

4. Harley, Vaughan: Brit. Med. Jour., 1897, i, 1218.

5. Volhard: München. med. Wchnschr., 1900, 5 and 6.

6. Stade: Untersuchungen über das fettspaltende Ferment des Magens, 1902. Braunschweig, Vieweg and Son.

7. Inouye: Archiv. f. Verdauungskrankheiten, ix, 326.

8. Falloise, A.: Arch. internat. de physiol. iii, 396-497.

9. Pesthy, Stefan v.: Arch. f. Verdauungskr., xii, 292; cited from Jahresb. u. d. Fortschr. d. Tierchemie (Maly), xxxvi, 363.

10. Sedgwick: Jahrb. f. Kinderh., lxiv, 194; Arch. Pediat., 1906, xxiii, 414.

be split to the extent of from 2.9 to 10.6 per cent. in the recovered gastric contents; and *in vitro*, using egg yolk emulsion according to Stade, it was found that as high as 24 per cent. of the fat was split in twenty-four hours. The acids recovered were mostly higher members of the series, insoluble in water and not volatile.

This work on the infants was very shortly confirmed by Heinsheimer.[11] Rietschel[12] did not find any fat-splitting power in the gastric juice from the Pawlow stomach of 8-day-old suckling pigs. Rietschel, however, expressly states that, because of the difficulty in collecting a sufficient working quantity from such small animals, the juice with which he worked was kept some hours or even days under toluol in the ice chest.

Ibrahim[13] found lipase to be absent in fetuses of 150 gm., 250 gm. and 780 gm., but present in small quantities in a fetus of 800 gm., and plainly present in those from 1,100 gm. upwards. The fat-splitting power was very strong in the glycerin extract of the gastric mucosa of a 9-months-old infant which died of pneumonia. Ibrahim's statement regarding the toluol is as follows:

"How can our positive results be brought into line with the negative findings of Rietschel and Engel? We believe it is the toluol that is to blame for the discrepancy. I know perfectly well that Sedgwick and Heinsheimer worked with toluol and got positive results. I suspect that they used but small quantities of toluol. We have been able to show, in a special series of experiments, that the toluol has a markedly inhibitory or completely suspending effect on the activity of lipase from the infant's stomach. It appears to act by an effect on the egg emulsion, for the juice which is freed from the excess of toluol by filter paper possesses fermentive activity. We used thymol. The addition of 2 per cent. sodium fluorid seems also not to be disturbing. We found later also that Laquer has noted this effect of toluol on the gastric lipase. I believe therefore that negative results which are gained in the presence of toluol should be considered of little importance."

This has been quoted in full to correct a mistake, and to call attention to an observation published by Sedgwick in 1906, which has not come to Heinsheimer's attention. The statement in Sedgwick's article,[10] that all his experiments were conducted under toluol, is an error which crept in after the manuscript left his hands, as such was not the case. In fact in the *Archives of Pediatrics*[10] the full data of an experiment showing the inhibitory action of toluol are given. Hecht[14] was able also to confirm the presence of a gastric lipase as well as the high per cent. of higher fatty acids which result from its action. The presence of lipase in the gastric juice of infants may therefore be considered to be established.

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11. Heinsheimer: Deutsch. med. Wchnschr., xxxii, 1194.
12. Rietschel: Monatschr. f. Kinderh., vi, 333.
13. Ibrahim: Verhandl. d. deutsch. Gesellsch. f. Kinderh., Koln, 1908, p. 36.
14. Hecht: Wien. klin. Wchnschr., 1909, 1404.

The presence of steapsin in the pancreatic juice of adults is so well known as to require no further discussion. Pancreatic steapsin has also been found in the infant.

As the gastric lipase acts on emulsified fat (Volhard), and as the food of the infant contains fat in an emulsified state only, the study of the fat ferment becomes of especial importance for the first year of life. It has been stated above that the fat-splitting in the stomach is limited in quantity. Considering these facts we began the study of the relationship between the gastric and pancreatic fat digestion.

In order to obtain gastric lipase entirely free from pancreatic steapsin we used the secretin from a Pawlow small stomach of a dog.[15] This was active, as the following results show:

Egg emulsion, 10 c.c., + thymol in chloroform were left in the incubator at 37 C. for twenty-four hours; 100 c.c. of ether were then added and the whole thoroughly shaken. After standing, 50 c.c. of the supernatant fluid were poured off and after the addition of phenolphthalein, required 1.2 c.c. n/10 NaOH for neutralization. A parallel experiment with the addition of 3 c.c. of the gastric juice from the Pawlow small stomach required 4.5 c.c. n/10 NaOH.

This shows a definite splitting.

In connection with the Schütz-Borissow law that the product of digestion is as the square root of the quantity of ferment, the following is of interest, as indicating that the splitting is due to a ferment. Treated as above:

One c.c. of Pawlow gastric juice split off 2.4 n/10, 4 c.c. of Pawlow gastric juice split off 4.9 n/10, almost exactly twice the amount, or $\sqrt{4}$.

Nine c.c. however required but 3 c.c., which may mean that the acidity became so high as to inhibit the action.

The technic of Donath[16] was then used, modified as follows:

Twenty c.c. of neutralized olive oil emulsion were held at 37 C. under varying conditions, as indicated in Table 1, and titrated at the end of stated intervals with n/10 NaOH.

As the experiments recorded in Table 1 show, the attempt was made to subject the emulsion in flask *b* to conditions similar to those in the body—that is, two hours under the influence of gastric juice, then neutralized and digested with pancreatic extract for three hours. The fatty acids produced required 66.1 c.c. n/10 as compared with 53.7 c.c. n/10 required in experiment *c*, which was not acted on preliminarily by the gastric juice. The amount of fat split was 23 per cent. greater when the emulsion was subjected to the gastric lipase before the pancreatic ferment. Control experiment *a*, in which neither ferment was used,

15. We are indebted to Dr. A. E. Wilcox for the skilful operation on the dog.

16. Donath, H.: Aktivierung u. Reaktivierung von Pankreassteapsin, Beitr. z. chem. Physiol. u. Path., 1907, x, 390.

TABLE 1.—EXPERIMENTS TO SHOW THE RELATIONSHIP BETWEEN GASTRIC AND PANCREATIC FAT DIGESTION

20 c.c. of emulsion+

	a	*b*	*c*	*d*
Water	7 c.c.	0	2 c.c.	5 c.c.
Gastric juice from stomach of dog	0	2 c.c. 2 hrs.	0 2 hrs.	2 c.c.
		Neutralized		
Pancreatic extract*	0 5 hrs.	5 c.c. 3 hrs.	5 c.c. 3 hrs.	0 2 hrs.
n/10 NaOH	9 c.c.	66.1 c.c.	53.7 c.c.	1.5 c.c.

20 c.c. of oil emulsion+

*The pancreatic extract was composed of commercial pancreatin and glycerin.

TABLE 2.—EFFECT OF BOILED GASTRIC JUICE ON COMBINED FAT-SPLITTING ACTION

Egg yolk emulsion, 10 c.c.

	a	*b*
Water	3 c.c.	3 c.c.
Juice from small stomach*	2 c.c. 2 hrs.	2 c.c. 2 hrs.
	Contents neutralized at end of 2 hrs.	Neutralized after 2 hrs.
Pancreatic extract	5 c.c. 3 hrs.	5 c.c. 3 hrs.
Titration n/10 NaOH	17.7 c.c.	20.1 c.c.

*Gastric Juice Boiled in *a* but not in *b*.

TABLE 3.—EXPERIMENT IN FAT-SPLITTING USING EGG YOLK EMULSION

Egg yolk emulsion 10 c.c.

	a'	*b*
Juice from small stomach	5 c.c. 2 hrs.	5 c.c. 2 hrs.
Water	0	5 c.c.
	Neutralized at end of 2 hrs.	Neutralized
Pancreatic extract	5 c.c. 3 hrs.	0 3 hrs
First titration: 100 c.c. of ether added to each, *a* and *b*, shaken and settled; supernatant fatty acid solution, 50 c.c. + 75 c.c. of alcohol requires for neutralization, n/10 NaOH.	7.3 c.c.	3.0 c.c.
Second titration of fatty acids from fat not split by the ferment	16.3 c.c.	20.0 c.c.
	23.6 c.c.	23.0 c.c.

TABLE 4.—EXPERIMENTS WITH EGG YOLK EMULSION, USING GASTRIC CONTENTS FROM AN INFANT

10 c.c. egg yolk emulsion+

	a	*b*	*c*
Gastric contents from an infant	5 c.c.	5 c.c.	0
	In the incubator 2 hrs.; alkalinized*	As *a*	
Pancreatic extract	0	5 c.c.	5 c.c.
	3 hrs. longer at 37 C.	As *a*	
100 c.c., ether added and titrated and as in Table 3—			
First titration n/10 NaOH	2.2 c.c.	6.8 c.c.	3.8 c.c.
Second titration n/10 NaOH (after saponification)	35.0 c.c.	30.2 c.c.	
	37.2 c.c.	37.0 c.c.	

*Neutralized + 2 c.c. NaOH.

could be neutralized by 0.9 c.c. n/10 NaOH. This shows the extent of the splitting due to the ferments. Control *d*, in which the gastric juice alone was used, shows that the inferior and slow action of the gastric lipase alone cannot account for the extent of the splitting.

In Table 2 it is shown that when the digestion is carried on with boiled gastric juice for two hours before the pancreatic extract is added the combined splitting action is lessened.

The two experiments tabulated in Table 3 were carried out as follows:

Egg yolk emulsion was used containing three yolks to 100 c.c. in both. To 10 c.c. of this fat emulsion, flask *a*, 5 c.c. of juice from the small stomach of the dog were added and kept in the incubator with thymol and chloroform for two hours. At the end of this time the digestion was neutralized and 5 c.c. of pancreatic extract were added. Flask *b* was treated in the same manner, with the gastric juice, but the pancreatic extract was omitted. Both flasks were again placed in the incubator for three hours, at the end of which time 100 c.c. of ether were added to each, and both were shaken and allowed to settle. Fifty c.c. of the supernatant fatty acid solution obtained were added to 75 c.c. of alcohol and titrated. Contents *a*, which had been subjected consecutively to both ferments, required 7.3 c.c. n/10 NaOH. Contents *b*, which had been acted on by the gastric ferment alone, required but 3 c.c., less than half as much.

The experiments in Table 4 were carried on as in Table 3, using gastric contents from an infant instead of the gastric juice from the small stomach of the dog. The egg emulsion digested with 5 c.c. of gastric contents for two hours, neutralized, and then rendered alkaline by the addition of 2 c.c. n/10 NaOH, and digested further for three hours, after being treated with ether and alcohol as before, gave a titration of 2.2 c.c. n/10.

When the pancreatic extract was added after the two-hour digestion with gastric ferment the titration was 6.8 c.c. n/10. When digested three hours with the pancreatic juice alone the titration was 3.8 n/10.

Gastric digestion alone five hours	2.2
Pancreatic digestion alone three hours	3.8
	6.0
Gastric digestion two hours alkalinized + pancreatic digestion three hours	6.8

From the above we feel warranted in concluding that the neutralization of the fat gastric digestion does not end the function of the gastric lipase of the dog or infant. Whether the effect shown is a summation of, or a relationship between, the actions of the two ferments, preparatory or activating, our results do not permit us to state with certainty. It seems justifiable, however, to conclude that the function of the gastric lipase of the infant is not ended when the gastric contents pass the pylorus and are neutralized in the duodenum.

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HIPPURIC ACID IN THE URINE OF NORMAL BREAST-FED INFANTS *

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The urine of the normal breast-fed infant is mainly distinguished by negative characteristics. This is a statement made by Mayerhofer[1] in his recent paper. In this paper attention is called to the absence of such substances as glycuronic acid, indican, urobilin, etc., in the urine of these individuals. According to the same author some of the products normally encountered in the urine of adults, like the substances paired with glycocoll, namely, benzoic acid, etc., have not been made the subject of detailed investigation. With regard to the occurrence of hippuric acid in the urine of infants, only a few scanty references came to our notice. Marchand[2] as well as Meissner and Shephard[3] state that the occurrence of hippuric acid in the infant's urine is a well-known fact. Amberg and Morrill,[4] examining 260 c.c. of a mixed urine obtained from several healthy breast-fed infants, were unable to demonstrate the presence of free or combined benzoic acid. From the examination of this amount of urine of such low concentration no definite conclusions could be drawn. It was therefore thought advisable to repeat the examination with a larger amount of urine. Thanks to the kindness of Dr. Williams of the Obstetrical Department, we were able to collect about 1,900 c.c. of urine from normal breast-fed infants. The amount obtained from the different babies was as follows:

Infant	Collection started, days after birth	Urine Collected, days	Amount collected, c.c.
1	10	2	409
2	6	6	426
3	6	6	914
4	23	2	162
			1,911

*From the Department of Pediatrics and the Department of Pharmacology, Johns Hopkins University.

1. Mayerhofer: Chemische Teilerscheinungen im Harne gesunder und kranker Säuglinge, Ztschr. f. Kinderh., 1911, i, 487.

2. Marchant: Ueber die Oxydationsproducte des Leims, etc., Jour. f. pract. Chem., 1845, xxxv, 309.

3. Meissner and Shephard: Untersuchungen über das Entstehen der Hippursäure; Hanover, 1866.

4. Amberg and Morrill: Ein Stoffwechselversuch, etc., Jahrb. f. Kinderh., 1909, lxix, 280.

The babies had surpassed their birth weight when the urine was collected and were in perfect condition clinically. To exclude the possibility of slight digestive disturbances 10 c.c. of each sample of urine was used for the determination of phosphoric acid. Moll[5] has shown that the amount of phosphoric acid excreted in the urine of breast-fed infants may serve to indicate very slight digestive disturbances. Only such urine was used as corresponded to the standard established by Moll for the urines of the class "free from phosphates." Therefore we have reason to assume that the urine examined by us was obtained from perfectly healthy individuals.

The method of analysis employed is that of Jaarsveld and Stokvis,[6] which was retested by Van de Velde and Stokvis.[7]

It is not our purpose to discuss here the literature concerning the occurrence of hippuric acid in the urine of animal and man under different conditions, nor the various methods for its determination. References to the literature may be found in the report of the United States Department of Agriculture.[8]

Each portion of urine was immediately evaporated to a small volume with the addition of some sodium carbonate, transferred to a flask and preserved with toluol until the total amount was collected. The method of analysis may be described briefly. The urine evaporated to a small volume is acidified with hydrochloric acid and thoroughly extracted with acetic ether after standing twenty-four hours. The acetic ether extract is washed with water and evaporated at room temperature, the residue containing free and combined benzoic acid, if any is present. The free benzoic acid is extracted with petrol ether. The residue is hydrolyzed by boiling with strong sodium hydroxid, thus liberating the benzoic acid from hippuric acid. After cooling, the fluid is acidified with hydrochloric acid and after standing over night, thoroughly extracted with petrol ether. This extract is evaporated at room temperature, leaving the benzoic acid.

Examined by this method, the urine did not show any crystals on evaporation of the acetic ether extract, nor was any benzoic acid found after the hydrolysis of the residue from this extract. There was no evidence of the presence of either free or combined benzoic acid. As with other methods of hippuric acid determination in urine, small amounts may escape detection. We may mention the statement of Wiechowski[9]

5. Moll: Die klinische Bedeutung, etc., Jahrb. f. Kinderh., 1909, lxix, 129.

6. Jaarsveld and Stokvis: Ueber den Einfluss der Nierenaffectionen, etc., Arch. f. exper. Path. u. Pharm., 1879, x, 268.

7. Van de Velde and Stokvis: Experimentelle Beiträge, etc., Arch. f. exper. Path. u. Pharm., 1883, xvii, 189.

8. The Influence of Sodium Benzoate on the Nutrition and Health of Men, Bull. 88, U. S. Dept. Agriculture, 1909.

9. Wiechowski: Die Gesetze der Hippursäuresynthese, Beitr. z. chem. Physiol. u. Path., 1906, vii, 204.

that the method of Jaarsveld and Stokvis gives good results even in the presence of small amounts of hippuric acid.

Since the question of the presence or absence of hippuric acid in the urine of the normal breast-fed infant is of considerable interest, it would have been desirable to extend our investigations with the employment of different methods of analysis, but we were unable to obtain the necessary amount of urine. Nevertheless, from the result just recorded it does not seem probable that a very appreciable part of the nitrogen contained in the urine of the normal breast-fed infant is excreted in the form of hippuric acid.

The character of the food—mother's milk, with its content of lactalbumin—is such that it could supply sufficient glycocoll for the formation of hippuric acid. But even if the food should not yield glycocoll on decomposition, this substance could be furnished by the animal organism. For instance, Grosser,[10] feeding young goats with casein and giving benzoic acid, found hippuric acid in the urine. Furthermore, Brugsch and Hirsch,[11] as well as Feigin,[12] found hippuric acid in the urine of hunger artists. To demonstrate that the normal breast-fed infant can readily furnish glycocoll, such a baby received 0.5 gm. of sodium benzoate. During the next twenty-four hours 175 c.c. of urine were collected, yielding, on evaporation of the acetic ether extract, hippuric acid.

The absence of demonstrable amounts of hippuric acid from the urine of the normal breast-fed infant depends, therefore, on the absence of benzoic acid. Most authors agree that the benzoic acid normally entering into the production of hippuric acid in man is either derived from benzoic acid or related substances contained in food, or from putrefactive processes in the intestinal canal.[13] Since it is known that putrefactive processes are, as a rule, in abeyance in the intestinal canal of perfectly normal breast-fed infants, the absence of hippuric acid from the urine would not be surprising. Quite recently Simon,[14] using the method of Henriques and Soerensen,[15] claims to have demonstrated the presence of hippuric acid in the urine of the breast-fed infant. In this method the hippuric acid is also extracted with acetic ether. The residue is

10. Grosser: Beitrag zur Bewertung des Albumingehalts, etc., Jahrb. f. Kinderh., 1911, lxxiii, 103.

11. Brugsch and Hirsch: Gesammt N, etc., Ztschr. f. exper. Pathol. u. Therap., 1906, iii, 638.

12. Feigin: Ueber die Hippursäurenscheidung, etc., Inaugural dissertation, Berlin, 1906.

13. See, for instance, Baumann: Die aromatischen Verbindungen, etc., Ztschr. f. physiol. Chem., 1886, x, 123; Gerhardt: Ueber Darmfäulniss, Ergebn. d. Physiol., 1904, iii, 138.

14. Simon: Zur Stickstoffverteilung im Urin des Neugeborenen, Ztschr. f. Kinderh., 1911, ii, 1.

15. Henriques and Soerensen: Ueber die quantitative Bestimmung, etc., Ztsch. f. physiol. Chem., 1909, lxiii, 27.

decomposed with hydrocholoric acid and the nitrogen of the resulting glycocoll is determined by means of the formol titration. In the first three days after birth the hippuric acid excretion was found to be rather high, running later on a lower level. The lowest figure was found on the eighth day (case Brunner), when 225 c.c. of urine yielded 0.005 gm. of nitrogen, corresponding to 0.0639 gm. of hippuric acid. The urine of our infants was collected later than the third day after birth; that is, when the excretion of hippuric acid has reached a lower level. If we calculate the amount of hippuric acid that should be present in the 1,911 c.c. of urine, using the lowest figure given by Simon, we should have 0.543 gm. of hippuric acid, or 0.37 gm. of benzoic acid. It is very unlikely that the urine examined by us should have contained an amount of hippuric acid approaching such a figure.

FURTHER OBSERVATIONS OF THE ACID CONTROL OF THE PYLORUS IN INFANTS*

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In a former paper[1] we recorded two experiments on the acid control of the pylorus in infants. We have since extended and verified these results and present them herewith, together with a partial description of the first experiments.

HISTORICAL NOTE

The explanation of the opening and closing of the pylorus was not fully made until Pawlow and Cannon's work was done. Not long after Beaumont's experiments in 1832 it is true that Hirsch, by means of a duodenal fistula in a dog, came to the conclusion that acid on the duodenal side caused the pylorus to close, but he abandoned his idea in favor of von Mering's observations, made about the same time, that the closure of the pylorus was due to the bulk of liquid or food in the duodenum. In his experiments von Mering introduces milk into the duodenum. The observation that the mechanical effect of inflating a small rubber balloon in the duodenum causes the pylorus to contract and its rhythmic movements to cease, seemed to lend support to von Mering's theory.

It was left for Pawlow and Cannon, however, to clear up these discrepancies and make full explanation of the phenomena observed by Hirsch and von Mering. Pawlow demonstrated that milk or neutral fat in the duodenum, whether in small or large bulk, excites the duodenal closing reflex and keeps the pylorus closed until the neutral fat has become saponified or until it has passed on into a lower segment of the intestine. He also showed that acid on the duodenal side closed the pylorus. Later Cannon demonstrated that acid in the stomach opens the pylorus and that the differential escape of carbohydrates and proteins from the stomach is due to their respective stimulating and combining property for hydrochloric acid. Hence the observations of Hirsch and von Mering were correct, but their explanations were entirely faulty.

AUTHORS' EXPERIMENTS

The experiments which resulted in the above observations were performed on dogs and cats. Of the various methods used Cannon's is

*From the Pediatric Clinic, University of Michigan.

*Read at the Meeting of the American Pediatric Society, Lake Mohonk, May, 1911.

1. Arch Pediat., February, 1911.

probably ideal, as it removed practically all abnormal conditions. In conducting our experiments we have been aware of the arguments against the accuracy of the method of tubing the stomach and we have not lost sight of the possible effect of the preantral sphincter on our results. The small size and the elasticity of the infant's stomach better adapt it for such observations than the adult stomach, and for these reasons we believe that the method we used, properly controlled, fully demonstrates the point at issue.

Method.—We selected babies who had proved their indifference to the passage of the tube. That is, they had become accustomed to the tube and retained it with perfect ease for any period desired. They would often sleep throughout an experiment, excepting for the brief interval of passing the tube. We found No. 14 (English) soft rubber catheter connected by a piece of glass tubing with a rubber tube and small bulb the most satisfactory apparatus for our work. As we had not investigated the effect of posture on the rate of stomach evacuation we had the position of the infant constant; that is, lying on the left side.

Control Test Meal.—Skim-milk, diluted one-half with water, was employed as a suitable test meal for these investigations. The meal usually contained a fraction of 1 per cent. of fat and proved more convenient to work with than milk containing a higher fat per cent., and this removed from discussion the possible effect of fat on the pyloric reflex. A definite amount was delivered to the stomach through a tube and allowed to remain a definite time. It was then recovered by expression and syphonage as described below.

Acid Meal.—This meal was prepared by treating skim-milk with dilute hydrochloric acid (10 per cent. solution) until the acidity desired was obtained. The food was then kept at body temperature for an hour to insure complete combination of the acid with the protein. It was then retested and treated, if necessary, to insure the acid value as it entered the stomach.

Basic Meal.—The basic calcium casein meal was prepared by adding the requisite amount of lime water to the skim-milk to render it faintly but distinctly alkaline to phenophthalein. The balance of the dilution was then made up with water so that, as with the control and acid meal, the skim-milk formed half of the mixture. This meal was also retested to insure its alkalinity as it entered the stomach.

Calculation of Error.—It could not be expected that work of this kind would be trustworthy for comparisons, excepting in marked differences. To ascertain what our error would be in infants who had not been previously tubed or selected for investigation because of their particular adaptability, we made sixteen observations on infants taken at random. These are recorded in Table 1. In most of these cases the infants were

allowed to go three and a half hours after a feeding before giving the test-water. If the stomach was empty we introduced 45 c.c. of plain water through the catheter, recovering it immediately by expression and syphonage. In each case the water was completely delivered to the stomach, none being allowed to remain in the tube. The syphonage was started by expression, one of us pressing over the epigastrium. It will be seen that our greatest error in recovering the contents is 5 c.c. and that the error is seldom greater than 3 c.c. In most instances a little mucus was recovered, As stated before, the infants with which this investigation had to do were carefully selected and caution was observed to wash and drain the stomach. In these babies our error[1] was less than 3 c.c.

TABLE 1.—SIXTEEN INVESTIGATIONS ON INFANTS TAKEN AT RANDOM TO DETERMINE ROUGHLY THE ERROR IN RECOVERING IMMEDIATELY BY MEANS OF STOMACH TUBE, A GIVEN AMOUNT OF FLUID DELIVERED TO THE STOMACH BY GAVAGE

No.	Name	Interval Since Last Feeding hours	Condition of Stomach	Amount of water Given, c.c.	Amount of water Recovered, c.c.	Condition of water Recovered
1	Edwards	3½	Empty	45	40	About ½ c.c. mucus
2	Hessler	3½	Empty	45	45½	.....
3	Rush	3½	Empty	45	46	A little mucus
4	Kinyon	2½	Empty	45	46	Tinged yellow
5	Wilcox	3½	Empty	45	41	.....
6	Rush	3½	2 c.c.	45	43	Few fine curds
7	Mills	3½	Empty	45	40	A little mucus
8	Hessler	3½	Empty	45	45½	Plugs of mucus
9	Simmons	3½	Empty	45	46	Considerable mucus
10	Hackford	3½	Empty	45	49	2 or 3 c.c. mucus
11	Hacket	3½	Empty	45	44	½ c.c. thick mucus
12	Rush	3½	Empty	45	41	Few fine curds
13	Hatzke	3½	Empty	45	40	Little thick mucus
14	Mills	3½	Empty	45	44	Few fine curds
15	Nering	3½	Empty	45	45	A little mucus
16	Hessler	3½	Empty	45	41	A little mucus

SERIES I.—THE EFFECT OF ACID ON THE DUODENAL SIDE OF THE PYLORUS

The three sets of experiments recorded in Charts 1, 2 and 3 have to do with the duodenal side of the pyloric reflex. The control meals enter the stomach, remain there for a certain time, until the acid reflex on the stomach side causes the pylorus to open. The acid meal enters the stomach with immediate stimulus for the pyloric opening reflex. As soon as it reaches the duodenum, in proportion to the amount ejected and its acidity, the pylorus remains closed. As our acid meal causes the pylorus to remain closed a comparatively long time, we speak of this as a sustained duodenal reflex, in contradistinction to the normal pyloric reflex and the delayed pyloric reflex recorded in our second series.

CASES 1 AND 2.—The data relating to these infants will be found in our previous report.[1] Both were in good health and gaining in weight. At no time

2. Greatest error in any one case 5 c.c. Average error 2.38 c.c.

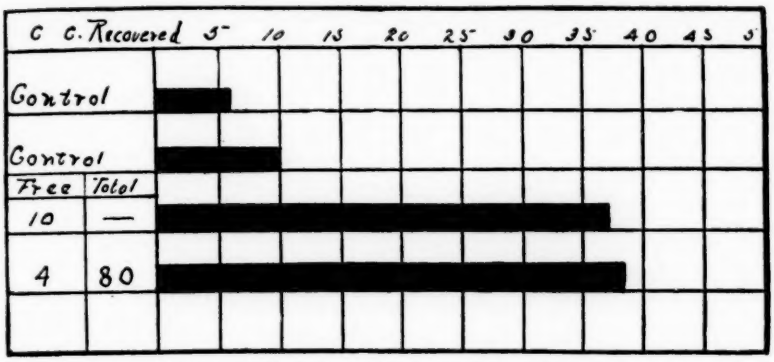

Chart 1.—Sustained duodenal reflex, Case 1.

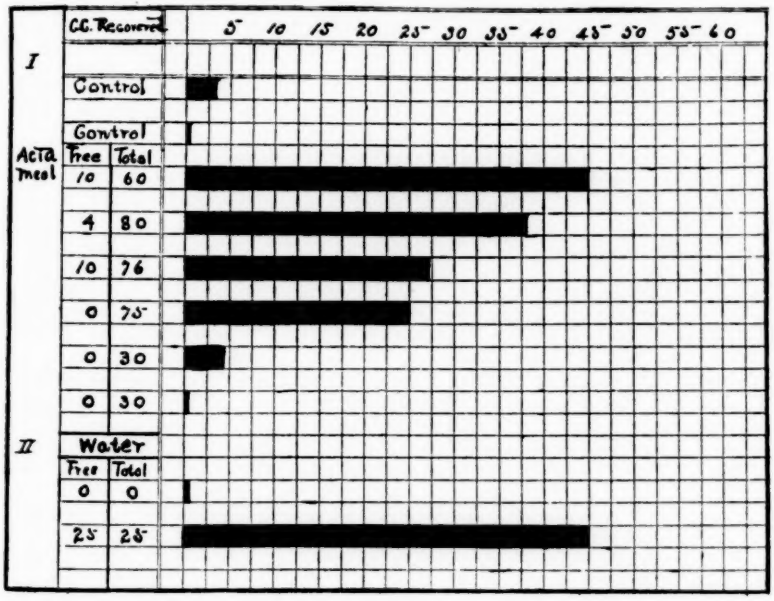

Chart 2.—Sustained duodenal reflex, Case 2. The secretion of this infant's stomach was always normal. There was no free HCl.

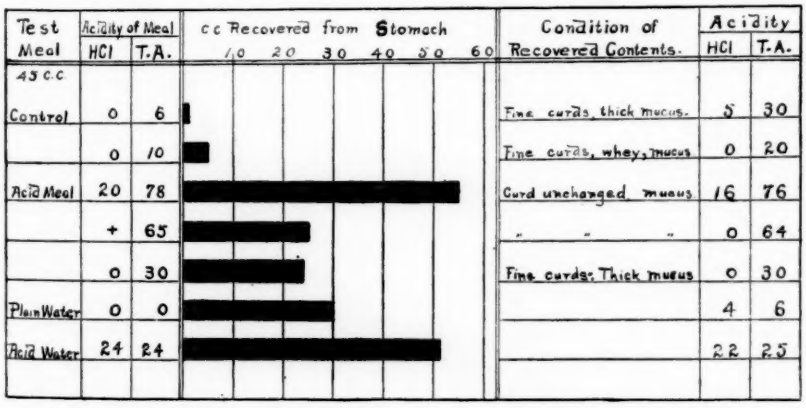

Chart 3.—Sustained duodenal reflex, Case 3. The secretion of this infant's stomach was always hypernormal. Free acid occurred in the fasting stomach.

in either case were we able to find any free hydrochloric acid. The delayed evacuation of the stomach is well shown in the acid meals. The higher the acidity, or the more acid present, the larger the amount recovered at the end of the period. This is particularly well shown in Case 2.

CASE 3.—A well developed baby. History and physical examination negative. On referring to the series of stomach analyses (Table 2) it will be seen that the infant almost always secreted acid to the free point and at times gave a free acid value as high as 25 and 35, a true hyperchlorhydria for an infant. In addition to this, there were evidences of hypersecretion during the period of our observations. How long such a condition would continue without producing spasm, if it ever would, we cannot say, as the infant soon passed from under our observation.

There was nothing in Case 3 to suggest ulcer, either peptic or duodenal. We find in this case, three hours after an ordinary feeding, when the stomach is practically free from food remains, a free acid value of 5. We also find that plain water leaves this baby's stomach much more slowly than does the control milk meal and the water meal in Case 2. It is believed, and supported by experiment, that water leaves the stomach almost directly. The reason for this, however, has never been satisfactorily explained. In this case we think the delayed evacuation of water can be explained by the presence of free acid in the fasting stomach and the hypersecretion. The water does not take up the acid but, as is known, may provoke a further secretion in this neurosis, hence the duodenal reflex is sustained longer than under normal conditions. In Case 2 we had no such condition to contend with. Free acid was never detected and the total acidity after an ordinary or test meal was never high, accordingly there was little or no neutralization to take place in the duodenum and the water passed on uninterruptedly into the gut.

TABLE 2.—RESULTS OF EXPERIMENTAL FEEDING IN CASE 3, SHOWING HYPERSECRETION AND HYPERCHLORHYDRIA*

Meal	Time in Stomach, Hours	Amount Fed, c.c.	Amount Recovered, c.c.	Free HCl	Total Acid
2-6-¾-W.	?	90	0	—	—
½ S. M. and water	¾	90	2	5	30
2-6-¾ W.	2	90	5	25	60
½ S.M. and water	¾	90	5	0	20
2-6-½-W.	2¾	90	4	35	70
2-6-½-W.	2½	90	7	35	70
Plain Water	¾	90	30	4	6
2-6-½-W.	?	90	2.5	15	60

*Abbreviations: 2-6-¾=2% fat, 6% sugar, ¾% protein. W=whey made up the balance of the mixture. ½ S.M.=Half skim milk and water.

DETAILED ACCOUNT OF EXPERIMENTS

Control Meal No. 1. Infant 36 Days Old. May 11, 1910

8:50 a. m. Three hours and fifty minutes after 90 c.c. 2-6-¾-whey mixture; nothing obtained through tube; stomach washed with 90 c.c. water; all recovered, containing about 1 per cent. fine curds and mucus.

8:55 a. m. Fed 90 c.c. half skim-milk and water, through a No. 14 catheter; total acidity of food; fat .9 per cent.

9:40 a. m. (45 minutes) 2 c.c. whey; mucus thick; a few very fine curds recovered; stomach washed with 85 c.c. water; 83 c.c. containing about 2 per cent. thick mucus and a few small curds recovered. Free HCl 5; total acid 30.

Control Meal No. 2. Infant 37 Days Old. May 12, 1910

8:40 a. m. Two hours and forty minutes after 90 c.c. of 2-6-¾ whey mixture; 5 c.c. recovered, containing 50 per cent. curds, and mucus thick. HCl 25; total acid 60. Stomach washed with 40 c.c. warm water; 40 c.c. recovered practically clear.

8:45 a. m. Five minutes later, fed by gavage 90 c.c. half skim-milk and water; total acid 10; fat .8 per cent.

9:30 a. m. (45 minutes) 5 c.c. recovered; whey containing a few small curds and mucus. HCl 0; total acid 20.

Acid Meal No. 1. Infant 38 Days Old. May 13, 1910

6:00 a. m. 90 c.c. 2-6-½ whey nursed.

8:45 a. m. 4 c.c. recovered, containing 25 per cent. thick mucus and a few small curds, HCl 35; total acid 70. Stomach washed with 45 c.c. warm water; all recovered, containing 2 per cent. thick mucus.

9:00 a. m. Fed 90 c.c., half skim-milk and water acidified by gavage. Free HCl 20; total acid 78.

9:45 a. m. (45 minutes) 55 c.c. milky material recovered containing 20 per cent. very fine curds and th.. nucus. The whey is very milky. HCl 16; total acid 76. Stomach washed with 45 c.c. warm water; all recovered; slightly opaque with milky material.

Acid Meal No. 2. Infant 42 Days Old. May 16, 1910

9:45 a. m. 90 c.c. half skim-milk and water, acidified, fed. Free HCl trace; total acid 65.

10:30 a. m. (45 minutes) 25 c.c. recovered. Same condition as when it entered stomach, excepting a little mucus. HCl 0; total acid 64. Stomach washed with 80 c.c. water; 82 c.c. recovered; slightly turbid.

Acid Water Meal Experiment. Infant 42 Days Old. May 16, 1910

6:00 a. m. 90 c.c. 2-6-½ whey nursed.

8:30 a. m. 7 c.c. recovered containing 50 per cent. thick mucus and curds. HCl 35; total acid 70. Stomach washed with 45 c.c. warm water; 46 c.c. recovered, slightly cloudy.

8:40 a. m. Fed 90 c.c. plain water by gavage.

9:10 a. m. 30 c.c. recovered containing a little thick mucus. HCl 4; total acid 6.

9:13 a. m. Fed 90 c.c. acidified water, HCl 24, by gavage.

9:43 a. m. (30 minutes) 51 c.c. recovered. Free HCl 22; total acid 25.

Acid Milk Meal No. 3. Infant 43 Days Old. May 17, 1910

8:55 a. m. 2.5 c.c. containing 60 per cent. thick mucus and curds recovered from stomach. Free HCl 15; total acid 60. Stomach washed with 95 c.c. warm water; 90 c.c. recovered containing 2 per cent. fine curds and mucus.

9:00 a. m. 90 c.c. half skim-milk and water, total acidity 30, given by gavage.

9:45 a. m. (45 minutes) 24 c.c. clear whey containing a few small curds and considerable thick mucus recovered. HCl 0; total acid 30. Stomach washed with 45 c.c. warm water; all recovered practically clear.

SERIES II.—THE EFFECT OF ACID ON THE STOMACH SIDE OF THE PYLORUS

In this series the control meal enters the stomach under the same conditions as before; there is a food stimulus for the secretion of acid to open the pylorus, while in the basic or alkaline meal, although the food stimulus, so far as we know, is exerted on the secretory mechanism of the stomach, the presence of alkali to the point of saturation of the protein delays the acid in reaching the point for stimulation of the opening reflex; hence at the end of forty-five minutes a very much larger amount is recovered than in the control experiments—not 5 or 10 c.c., but double and treble the amount.

It will be observed in these experiments that at times we recovered as much as 15 c.c. more, at the end of the period, than we had put in. This was at a time preceding the opening reflex and represents roughly the amount of gastric juice secreted. In Case 4 we recovered at the end of thirty minutes 15 c.c. more than we put in; at the end of forty-five minutes we recovered a few c.c. more than we originally put in, but about 12 c.c. less than we reintroduced into the stomach. In this experiment, if we had again introduced the contents removed at forty-five minutes, ten minutes later we might have experienced what we have on more than one occasion—the stomach almost empty. The pyloric reflex has just begun to operate and because of the low acidity of the food either a large gush or a series of rapid short gushes has evacuated the stomach. On one occasion at forty-five minutes nearly all the food was present in the stomach, and no curd formation had taken place; in fifty minutes only a small amount of curded material could be recovered.

These experiments, we think, give abundant proof that the pylorus is governed by acid on both sides of the pyloric ring and confirm, in man, the experiments in animals done by Pawlow, Cannon and others.

CASE 4 (Charts 4 and 5).—Baby G., an apparently normal infant. History and physical examination negative. On referring to the series of stomach analyses, Table 3, it will be seen that this infant never secreted free acid and that the total acid was never excessively high.

TABLE 3.—RESULTS IN FREE HCl AND TOTAL ACIDITY IN FEEDING EXPERIMENTS IN CASE 4

Meal	Time in Stomach, Hours	Amount Fed, c.c.	Amount Recovered c.c.	Free HCl	Total Acidity
2-6-½	1¾	75	27	0	32
½ S.M. and Water	¾	45	13?	0	26
2-6-½ W.	2¾	45	26	0	32
½ S.M. and Water	5/6	45	?	0	15
2-6-½ W.	½	30	30	0	44
2-6-½ W.	2¾	90	1	0	—
½ S.M. and Water	⅔	45	?	0	12
2-6-½ W	...	..	..	.	..

DETAILED ACCOUNT OF EXPERIMENTS IN CASE 4

Control Meal No. 1. Infant 30 Days Old. May 25, 1910

7:30 a. m. Nursed 75 c.c. 2-6 ½ mixture.

9:13 a. m. 27 c.c. recovered, containing 15 per cent. curds and thick mucus. HCl 0; total acid 32. Stomach washed with 90 c.c. water; 90 c.c. recovered, containing 2 per cent. curds.

9:20 a. m. 45 c.c. half skim-milk and water, total acidity 10, given by gavage.

9:50 a. m. (30 minutes) 13 c.c. of fluid were expressed, consisting of whey, medium sized curds, and thick mucus. This was returned to the stomach.

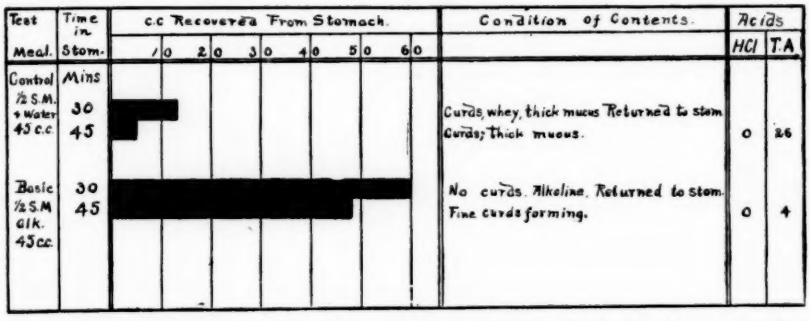

Chart 4.—Delayed pyloric reflex. Case 4, Experiment 1, showing the effect of alkali on stomach evacuation. The secretion of this infant's stomach was always normal.

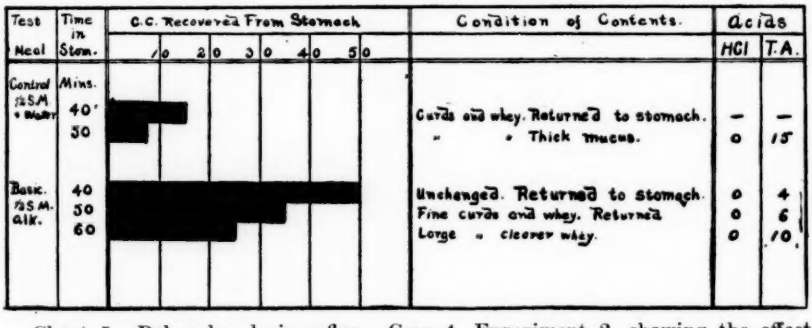

Chart 5.—Delayed pyloric reflex. Case 4, Experiment 2, showing the effect of alkaline contents on stomach evacuation.

10:05 a. m. (45 minutes) 15 c.c. of fluid were expressed consisting of 20 per cent. large curds and some thick mucus. HCl 0; total acid 26. Stomach washed with 90 c.c. water; 88 c.c. returned practically clear.

Basic Meal No. 1. Infant 30 Days Old. May 25, 1910

10:10 a. m. 45 c.c. of half skim-milk and water, rendered basic with lime water, were given by gavage.

10:40 a. m. (30 minutes) 60 c.c. recovered; no curds; reaction alkaline to litmus; returned to stomach.

10:55 a. m. (45 minutes) 49 c.c. Fine curds beginning to form. HCl 0; total acid 4. Stomach washed; only a few fine curds returned.

Remark: It will be observed that thirty minutes after feeding we recovered 15 c.c. more than was introduced, and that no curd formation was present; that fifteen minutes later curds had formed and 45 c.c. were recovered. No stimulus to pyloric opening was present until about this time. The 15 c.c. doubtless represents grossly the amount of gastric juice secreted during the first thirty minutes' stay in the stomach. See Chart 4.

Control Meal No. 2. Infant 32 Days Old. May 27, 1910

6:00 a. m. Fed 45 c.c. 2-6-½ whey mixture.
8:40 a. m. 26 c.c. recovered; 30 per cent. curds and thick mucus. HCl 0; total acid 32. Stomach washed with 90 c.c. warm water; all recovered, containing a little over 1 per cent. fine curds and mucus.
8:45 a. m. 45 c.c. half skim-milk and water, total acid 9, given by gavage.
9:25 a. m. (40 minutes) 15 c.c. expressed, consisting of fine curds and whey. Returned to stomach.
9:35 a. m. (50 minutes) 8 c.c. fluid containing 20 per cent. medium small curds and a little thick mucus recovered. HCl 0; total acid 15. Stomach washed with 90 c.c. water; 89 c.c. recovered, containing a few fine curds and mucus hardly measurable by centrifuge.

Basic Meal No. 2. Infant 32 Days Old. May 27, 1910

9:40 a. m. 45 c.c. one-half skim-milk and water, rendered basic with lime water, were given by gavage.
10:20 a. m. (40 minutes later) 50 c.c. recovered; no distinct curds; appears about the same as when introduced. Total acid 4; returned to stomach.
10:30 a. m. (50 minutes) 35 c.c. recovered; distinct fine curds and whey. Free acid 0; total acid 6. Returned to stomach.
10:40 a. m. (60 minutes) 25 c.c. recovered; curds larger and more separated from the whey. HCl 0; total acid 10. Stomach washed clear.

Basic Meal No. 3. Infant 36 Days Old. May 31, 1910

5:00 a. m. 75 c.c. 2-6-½ whey mixture.
8:00 a. m. 15 c.c. 2-6-½ whey mixture.
8:30 a. m. 30 c.c. of whey containing 2 per cent. curds and a little thick mucus recovered. HCl 0; total acid 44. Stomach washed with 130 c.c. warm water. All recovered plus a little mucus.
8:55 a. m. 45 c.c. one-half skim-milk and water, rendered basic, given by gavage.
9:35 a. m. (40 minutes) 35 c.c. recovered, containing 20 per cent. curds, whey and thick mucus. Tube was repeatedly blocked by the curds. HCl 0; total acid 8. Stomach washed with 90 c.c. warm water; 90 c.c. recovered, containing a few small curds and considerable thick mucus.

Control Meal No. 3. Infant 38 Days Old. June 2, 1910

6:00 a. m. 90 c.c. 2-6-½ whey mixture.
8:45 a. m. 1 c.c. thick mucus recovered. HCl 0. Stomach washed with 45 c.c. warm water; all recovered, perfectly clear excepting a little mucus.
8:55 a. m. 45 c.c. plain one-half skim-milk and water were given by gavage; total acidity 8.
9:15 a. m. (20 minutes) 45 c.c. recovered; fine curds beginning to form. Returned to stomach.
9:25 a. m. (40 minutes) 30 c.c. recovered; curds more distinct; mucus more marked. Returned to stomach.
9:35 a. m. (50 minutes) 15 c.c. recovered, whey containing 5 per cent. large curds; tube blocked with thick mucus. HCl 0; total acid 12. Stomach washed clean.

It may be asked what practical bearing these observations have on gastro-enterologic therapy and on our knowledge of gastro-enteric diseases. It was Dr. Cowie's object in starting these observations to see if the management of pyloric stenosis in infants, both true and false, could be put on a scientific basis. Most cases of this character have been treated without reference to the pyloric reflex or the altered physiologic conditions present. We believe there is a certain group of cases in which these are important factors to determine. It would seem at least possible to recognize varying degrees of stenosis and readily to differentiate them from what may be called pseudo-stenosis or spasm and to enable us to observe the effect of the reaction of the food given on the duration of the duodenal closing reflex, which seems to be an important factor in many cases. This will be considered in a later article.

CONCLUSIONS

1. The pyloric opening and closing reflex can be easily demonstrated in infants' stomachs.

2. In experimental acid stomach contents the duodenal closing reflex is sustained and consequently the evacuation of the stomach is delayed.

3. In experimental alkaline stomach contents the pyloric opening reflex is delayed and consequently the evacuation of the stomach is delayed.

4. Free acid is not necessary for pyloric opening. Its presence has a tendency to provoke prolonged duodenal closing in an infant.

5. In hypersecretion in infants protein-containing food appears to leave the stomach more readily than water because of its binding property for acid.

Lawrence Building.

THE RELATION OF MEAT INGESTION TO INDICANURIA IN CHILDREN *

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With the view of gathering, if possible, some data on the use and abuse of meat diet in childhood, the work reported in this paper was begun about a year ago. It was hoped that the results of the experiments might lead to some definite indications as to the quantity and frequency with which this article of diet should be allowed.

So much work has been done on the dietetic requirements of infancy, and from both theoretical and practical standpoints so many valuable conclusions have been drawn, that it seems strange that more work has not been done to settle the same problems in older children.

The insidious, often marked, symptoms that chronic dietetic disturbances show after two years of age, compared with the more acute signs of intestinal indigestion in infancy, probably account for the rather neglectful attitude that even pediatrists have taken toward regulating the diets of older children.

If one makes it a practice to discuss with his patients their attitude towards the giving of meat to children, he will find as a rule that one of two rather disagreeable conditions exists. Either the child receives no meat at all, the parents laboring under the only too frequently met delusion that meat soups contain all of the valuable constituents of the food, or that the child receives meat twice or even three times a day. It is a question which of these two evils is the worse. The one that puts on the kidneys the duty of excreting a wealth of useless extractives, or the one which forces on the youthful organism three meals a day—more than sufficient to supply the caloric needs of a working adult. One thing is definite, however, and that is that if the next generation of men and women is to be a healthy one we must so regulate the conditions under which the children live that their growth may not be impeded by chronic intestinal disturbances.

During the past two years a large number of stools has been examined incidental to routine investigation, and while it has been strikingly common to find free starch and free fat, especially in those children with clinical symptoms of intestinal disturbance, it has been rather sur-

*Read in the Section on Diseases of Children at the Sixty-Second Annual Session of the American Medical Association, held at Los Angeles, June, 1911.

prisingly rare to find undigested muscle-fiber, except in the most marked cases. Bearing this in mind, and desiring, if possible, to reach some conclusion as to the advisability of giving meat to children over two years of age, it was decided to investigate the pathologic products which the urine might contain, which might have some bearing on this subject.

Taking into consideration that an excess of meat in the diet would probably lead to improper digestion and consequent putrefaction, it seemed reasonable to assume that the amount of indican in the urine of children fed on small and large quantities of meat might throw some light on the subject.

Appreciating the fact that under normal circumstances little or no indican is excreted in the urine, it seemed possible that if meat were given in excess, digestion would be sufficiently interfered with to allow the putrefactive bacteria to act on the excess of protein, and the indicanuria would be a gauge as to the ability of the organism to properly handle the animal food.

It is almost universally conceded now, as Nencki and others have shown, that indol, the forerunner of indican, is produced in the intestine solely by bacterial putrefactive decomposition of the protein food. There have been a few dissenters from this view, notably, Flint, who states that it may be formed by the action of the tryptic ferment of the pancreatic juice on the protein food. Herter states that such a phenomenon could only occur in the intestines in the presence of excessive amounts of protein food combined with greatly delayed digestion. Ordinary absorption occurs in the peptone and amino-acid stage of proteolytic digestion and it is hardly conceivable that a rapidly proteolyzed meal should lead to the formation of indol. In unmistakable and most conclusive support of the bacterial putrefactive source of indol, stands the work of Senator, who in a large number of investigations failed to detect the merest trace of indican in the urine of new-born babies, the stools of which are always bacteria-free.

The object in selecting indican as the urinary by-product, which might throw some light on the use of meat diet in childhood, was twofold. First, because it has been definitely proved that one of the chief causes of indicanuria is an excess of food, which by hampering digestion allows the putrefactive bacteria to work, and second, because it seemed advisable, if possible, to have some single test that might be of use to the ordinary practitioner.

That accurate nitrogen and sulphur determinations may in the future throw some light on this very interesting subject is probable, but this does not come within the province of anyone but the trained chemist and is therefore of little value in aiding the clinician.

The minute details of a well-planned piece of investigation which one can carry out successfully in a properly organized laboratory, are not within the power of the best intentioned worker when he has to deal with institutional children as the objects of his experiments; and when, furthermore, he has to depend on the gracious willingness of institutional attendants to carry out instructions as to diets, he is truly in a dilemma that is discouraging. On account of this difficulty, which is practically unsurmountable, it seemed advisable to pursue the work without disturbing the routine of the home from which the specimens were obtained, knowing that quantitative diets could not be given, and that only untrained assistants would have to be depended on to furnish the daily specimens of urine. The diets given to the children corresponded to the diets usually given to children in the ordinary orphanages and no attempt was made to modify this under the first series of tests that was carried out.

A brief résumé of this diet may be *apropos* in order that one may understand fully the most important factor in determining the conclusions. For breakfast: fruit, cereal, toast and milk. Dinner: milk soup, meat, potatoes, green vegetable, and dessert. Supper: bread, milk and fruit. The diets were somewhat variable as to the particular kinds of cereals, meats and vegetables, but otherwise were fairly constant.

With the object in mind of determining the influence which age had on the ability to digest meat, it was decided to divide the children into four groups. In the first group were six children 12 years of age. In the second group, six children 9 years of age. In the third group, six children 6 years of age, and in the fourth group, six children 3 years of age. The early morning urine was the sample tested in each case and the Obermayer test was the one employed in formulating the results.

A rather arbitrary method was used for designating the quantity of indican present in each specimen, + representing a moderate reaction, ++ a marked reaction, and +++ a very marked reaction. The children on whom the tests were made were normal children as far as physical examination could determine. In each case the urine was carefully examined in order to exclude pathologic conditions of the kidney, and no child was observed in whom the urine showed the slightest deviation from the normal.

In the first group of children tested were six normal girls, 12 years of age, in each of whom twenty-five specimens of urine were examined, making a total of 150 experiments, in fifteen of which on different days a single + reaction was obtained. In other words, 10 per cent. of the specimens of urine of 12-year-old institutional children showed a moderate reaction for indican, indicating a slight amount of intestinal putrefaction with the diet which they were receiving.

In the second group of children were six girls 9 years of age. One hundred and fifty specimens of urine were tested and twenty of them showed a single + reaction with the routine diet, a slight increase (13 per cent. as compared to 10 per cent.) over the number of positive reactions among the 12-year-old children but not sufficient to warrant any deduction.

In the third group of children were six girls 6 years of age. One hundred and fifty specimens of urine were examined and in about 15 per cent. of the examinations a single + reaction was obtained.

In the fourth group were six children 3 years of age, and the results here were decidedly interesting because they showed that in children of this age the amount of protein food received in an ordinary diet containing milk and meat once daily gave rise to considerable intestinal putrefaction and indicanuria. Twenty per cent. of these examinations showed a moderate single + reaction and 15 per cent. gave a marked + + reaction. In all of the cases under observation, one or more normal bowel movements occurred every day, so that constipation could in no way have had an influence on the results.

These experiments, which were made with the children receiving ordinary diets, were now repeated after the children had been given meat twice daily for two weeks. The instructions given were that the children under observation should receive the same diets as previously, except that they should receive in the evening the same quantity of meat as at noon. In the 150 tests made on the urine of the 12-year-old girls, 2 per cent. showed a marked double + + reaction and 12 per cent. showed a moderate single + reaction. The results were practically identical with those obtained when the children were getting meat but once daily. In the 150 tests made in the second group of children 9 years of age, 14 per cent. showed a moderate single + reaction, these results also being practically the same as when the children were getting meat only once daily.

In the observations made on the 6-year-old children who were receiving meat twice daily, the results were rather more striking. Twenty-five per cent. showed a moderate single + reaction for indican and 15 per cent. showed a marked double + + reaction. This was a decided increase in the number of positive reactions—25 per cent. of moderate single + reactions as compared with 15 per cent. and 10 per cent. of marked double + + reactions as compared with no + + reactions when the children were receiving meat but once daily.

In the 3-year-old children the results were also very striking. Thirty-five per cent. of the reactions were single + or moderate reactions and 30 per cent. were double + + or marked reactions as compared with

20 per cent. of moderate reactions and 15 per cent. of marked reactions in these same children when they were receiving meat but once a day.

The results, while strongly suggestive, and while warranting one in advocating certain principles in the feeding of children, might be criticized on the ground that the conclusions are not based on the observation of a sufficiently large number of children. Admitting this, still the absolutely negative results in the 9- and 12-year-old children, with the positive results in the 3- and 6-year-old children are very suggestive.

A brief résumé of the results obtained shows as follows:

1. With an ordinary diet containing meat once daily, children 6, 9 and 12 years old succeed in digesting their food fairly well without much putrefaction in the intestinal tract. Three-year-old children, on the other hand, with the same diet are much more apt to show indicanuria.

2. The giving of meat twice daily produces in 9- and 12-year-old children practically no change in the amount of intestinal putrefaction.

3. In 6- and even more markedly in 3-year-old children meat given twice daily gives rise to a decided increase in the indicanuria and is a cause of pronounced intestinal putrefaction.

4. As limited as these observations may be, they seem to point to one definite conclusion, and that is that the giving of meat more than once daily to children under 9 years of age is a practice conducive to intestinal putrefaction and indicanuria, and is to be deprecated on account of the harm resulting to the organism from the constant presence of abnormal products of putrefaction.

350 Post Street.

THE TREATMENT OF CHRONIC NEPHRITIS IN CHILDREN BY THE EDEBOHLS OPERATION *

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The treatment of chronic forms of nephritis by an operative procedure of splitting the capsule of the kidney was first proposed by Edebohls and advocated by him as a mode of curing ultimately the disease of these organs and restoring them to normal condition, that is, of curing the nephritis. In his list of seventy or more cases of nephritis he reports seventeen patients as permanently cured; that is, casts and albumin had disappeared from the urine, and the patients were fully restored.[1] However this may be, I have not undertaken the treatment of the cases which form the basis of this paper with any such purpose in view. It can scarcely be conceived that an organ so irreparably damaged as those of any of my patients could be restored to its original integrity. The object for which I submitted the patients referred to in this paper to operation was less ambitious and still humane. In children no disease subjects the victim to more suffering than chronic incurable disease of the kidney. The general anasarca alone makes a species of bedridden sufferer of the little one, and anything or any operation which would eliminate this one symptom and enable the patients to take their place among the apparently well would and must receive more than passing notice. It should be remembered that of the five cases here recorded all of the patients were chronic invalids, four for very long periods of time; some of the patients had been repeatedly in the hospital to be treated for recrudescences of symptoms. All of the patients for a length of time extending over months had been subjected to other forms of treatment, having in view a relief of the distressing symptoms of anasarca and uremia, and all these forms of treatment had failed, not on account of any lack of persistence in treatment, but because it was impossible to make the crippled organ respond to any known forms of medical management.

Under these conditions and in face of the fact that the patients were chronic bedridden invalids, the Edebohls operation was performed simply in the hope of relieving the anasarca and restoring the patients to an

* Read before the Association of American Physicians, May, 1911.

1. There was only one case in Edebohls' series of a child who was operated on. Whether this is the same child reported by A. Caillé in the Transactions of the American Pediatric Society, Vol. xiv, I cannot say. The number of cases in the literature of children suffering from nephritis who have been operated on by the Edebohls operation and subsequently studied are exceedingly few.

existence at least simulating health. This was attained in four of the five patients operated on. In three cases the return after the severe operation to a condition of ambulatory well-being was gratifying; one patient was lost sight of after being in excellent condition fully a year, and the fifth died as a direct result of the failure of the operation to cause a response on the part of the kidneys. In no case could it be said that the operation endangered life. Drs. Lilienthal and Elsberg were the surgeons who readily supported the idea of subjecting the patients to this operation at my suggestion. The operation is in itself well borne by the patient and the recovery from the so-called shock and anesthetic is very prompt indeed.

REPORT OF CASES

CASE 1.—H. R., male, aged 11, was admitted October 15, 1905.

Family History.—Father, mother and two other children alive; no history of renal disease in the family.

Previous History.—Measles at 3 years; scarlet fever at 4 years. Three months after the scarlet fever the patient had swelling of the face for a few days, which disappeared spontaneously; had headache about every two weeks since his attack of scarlet fever. At these times he felt nauseated, usually vomited and then felt better. There was no history of rheumatism, malaria, typhoid, ear disease or jaundice; no cardiac history.

Present Illness.—This began two months ago; mother first noticed swelling of the boy's face. He had suffered no unusual exposure. A few days later swelling of the abdomen was noticed and again in a few days edema of the feet became prominent. At first there were no subjective symptoms. Later the child complained of slight dyspnea; occasionally there was vomiting and abdominal pain. These symptoms continued until admission. For the previous eight days the vomiting had been severe, the patient vomiting almost everything he ate; had been constipated for a week and had passed very little urine. There was no change noticed in the amount of urine he passed until one week previous to admission. Appetite was poor; had no spots before the eyes; headache had not troubled him recently.

Physical Examination.—General condition good; well nourished.

Skin: Pale, slight puffiness of cheeks and lower eyelids.

Eyes: Pupils negative; scleræ very white.

Mouth and Throat: Teeth and gums in fair condition; tongue moist and slightly coated; throat, negative.

Glands: Considerable glandular enlargement in axillary regions; moderate enlargment in posterior cervical, submaxillary, epitrochlear and inguinal regions.

Lungs: Anteriorly and posteriorly over both chests were heard sibilant sounds with expiration. From the angle of the scapula to base, both sides posteriorly exhibited dulness, diminished fremitus and diminished breathing. Anteriorly there was a hyperresonant note over both chests.

Heart: Borders difficult to determine because of hyperresonance of chest; does not appear to be enlarged; apex beat not seen or felt; slight impurity of first sound at apex; moderate accentuation of both two-inch basic sounds, especially aortic; action regular, forcible, about normal in frequency; no murmurs.

Pulses: Equal, normal in force and frequency, rather large, regular; slight increase in tension.

Spleen: Not palpable.

Liver: Fourth space to sixth space to free border; not palpable.

Abdomen: Generally tympanitic; too tense for satisfactory palpation; not tender.

Lower Extremities: Knee-jerk markedly exaggerated; slight edema of legs.
Genitals: Negative.
Rectal: Negative.

October 27: The diagnosis was post-scarlatinal nephritis (large white kidney). There were pallor, puffiness of cheeks and lower-eyelids, signs of a moderate double hydrothorax, moderate soft edema of the legs and feet, accentuation of the second sound at both basic cardiac orifices, slightly increased pulse tension and considerable albumin, and hyaline and a few hyalo-granular casts in the urine. A fair amount of urine and urea was being excreted.

November 22: The various well recognized modes of treatment were found unavailing in this case. The anasarca persisted; no improvement in the renal condition as judged by the urine; there were still present pallor, puffiness of the cheeks, hydrothorax, ascites, considerable soft edema of the legs and feet, considerable albumin, casts and some red blood-cells in the urine; tongue moist and coated. Posteriorly on the left side of the chest, dulness began at the middle of the scapula, and became flatness, with fremitus and breathing at the base, diminished voice, breathing and fremitus over the dull area; similar signs though slightly less extensive on the right side. The heart, except for marked accentuation of second basic sounds, was negative. The left ventricle, however, seemed somewhat enlarged, the left border being outside the nipple line; abdomen gave signs of moderate amount of ascitic fluid; edema of penis and scrotum had increased.

November 23: *Operation.*—Decapsulation of kidneys for subacute nephritis by Dr. Lilienthal.

Right: Incision was made from just below border of ribs posteriorly, obliquely downward and forward toward ant-superior spine of ilium. On incising the subcutaneous tissue, a great amount of serous fluid exuded and the tissue appeared gelatinous. The muscular tissue appeared very pale and edematous. Incised between fibers of oblique muscles, and found that the incision was made entirely too high. Therefore, an incision was made through the skin downward and at right angles to first oblique incision. The muscles now retracted, the fatty capsule of kidney was incised and the kidney palpated high up under the ribs. With some difficulty the kidney was delivered into the wound. The capsule was incised along the posterior border and slipped easily from the kidney on each side to the pelvis of the kidney. The kidney was about twice the usual size. It was replaced and the muscles sutured with No. 2 chromic gut, by interrupted sutures in two layers. Drain to kidney and at lower angles; silk for skin.

Left: Oblique incision was made the same as above. Subcutaneous tissues and muscles presented same appearance as on right side. The fatty capsule was incised and kidney delivered into wound; it was found about one and one-half times its usual size. Capsule of kidney incised along posterior border and capsule stripped to pelvis on each side, but capsule seemed somewhat more adherent than on right side. Muscles sutured.

November 26: Following the operation patient passed about ℥xx of urine in twenty-four hours. The general condition was no worse than previous to the operation. The patient was comfortable, took his nourishment well, did not vomit, had no pain. The temperature had not been above 101 F., pulse of good quality. There was a profuse serous discharge from the wounds. On this date there was some increase in the edema; legs markedly edematous, ascites increased; signs of hydrothorax unchanged; considerable edema of scrotum and penis; acupuncture of scrotum and prepuce performed.

December 2: During the previous two weeks the ascites and anasarca were about the same as previous to the operation. Amount of urine passed in twenty-four hours was from ℥viii to ℥xiii. The discharge from the wounds, however, had a uriniforous odor, and probably considerable urine was excreted directly from the wound.

December 28: For the previous few days patient had been running a temperature (maximum 105 F.). He had been passing very small quantities of urine

(9-10⅗ during twenty-four hours). The edema of the face, abdomen, legs, penis and scrotum had increased. He complained of pain in the lumbar region and legs. There had been no headache or vomiting. The urine contained much albumin and a moderate amount of hyaline and granular casts.

January 1, 1906: Multiple puncture of penis and scrotum was done and wet dressing applied.

January 5: Since December 30 the patient's temperature had been normal. He had been passing fair amount of urine, which now contained only a trace of albumin, and a few hyaline and granular casts. The general condition was much improved. The anasarca was diminishing. There were no uremic symptoms. Patient was on soft diet.

January 19: The previous fourteen days the patient had been passing a small amount of urine. Puffiness of face and ascites had increased, but there was no increase in the edema of the legs. There had been no rise in temperature. The urine did not contain macroscopic blood, but only some red blood-cells. On this date the urine looked bloody and contained a great many blood cells, a great deal of albumin and hyaline and granular casts; also some pus and epithelial cells. Aside from the change in the character of the urine, the patient's condition had not changed. He was comfortable and had no vomiting, pains or cardiac palpitation, or any other uremic symptom.

January 27: There had been improvement in the patient's condition in the previous six days. He had been passing sufficient urine, which contained no macroscopic blood, but contained some albumin, hyaline, hyalogranular and granular casts and red blood-cells in moderate amount, about 2 gm. in twenty-four hours. Edema of face, ascites, edema of scrotum, prepuce and legs had disappeared entirely. There were no uremic symptoms.

February 22: Patient complained of sore throat and difficulty in swallowing. On inspection the throat was found to be reddened, the tonsils somewhat swollen, and there were a few enlarged and slightly tender lymph-nodes in the left submaxillary region. The temperature February 21 rose to 100.8 F. (it had not been above 100 for eleven days); February 22 it was 100.4 F. Aside from the angina, the patient was comfortable. The urine showed no change; it was alkaline, sp. gr. 1,028, contained albumin and a moderate number of hyalogranular casts, some red blood-cells and pus-cells.

March 9: General condition good; no edema; lungs negative; heart borders unchanged; second sound at base very slightly accentuated; pulse equal, good force, regular, no increase of tension. The urine showed a moderate number of very small hyaline casts, few pus-cells, and few red blood-cells.

March 24: Urine still contained pus, albumin and a moderate amount of hyalogranular casts; no red blood-cells. There was no edema, no dyspepsia, no tension. Discharged very much improved.

November, 1906: Patient continued in very good physical condition, without any edema or symptoms. A single fresh specimen of the urine was examined; it was alkaline, amber, and contained albumin, a moderate number of granular casts, epithelial cells, leukocytes and numerous red blood-cells.

April 28, 1906: The patient was in good condition; no symptoms; well nourished, rather pale, no evidences of cyanosis or dyspepsia; nothing suggestive of nephritis about facies. Heart showed some hypertrophy to the left of the apical impulse; strong second pulmonic accentuation; no edema; urine 1,020; contained casts and epithelial cells, but no red blood-cells; the number of formed elements was small in proportion to the albumin, which was large; pulse was regular, increased in tension.

May 26, 1906: Urine 1,026, acid, positive for albumin and contained hyaline, hyalogranular and granular casts, leukocytes and epithelium.

This case gives a history of a nephritis of at least seven years' standing, with a culmination of symptoms three months before ultimate

operation, and a failure to respond to therapeutic measures which would enable the patient to be up and about. It should be noted that the improvement did not set in immediately, but was delayed, with even increased anasarca and diminution of urine for six weeks after the operation, when improvement set in and was progressive. The improvement was permanent and continued after operation, which, in view of the fact that this boy was not particularly well taken care of and was exposed to all kinds of weather, was certainly satisfactory.

CASE 2.—A. R., male, aged 6 years, was admitted in July, 1902.

Family History.—Negative.

Previous History.—No infectious diseases except scarlet fever three and one-half months prior to admission, which was complicated with nephritis; anasarca was general, urination diminished and the child had convulsions.

Present History.—This dates from this illness. Since the first acute attack the patient had never been well; had headache, diminished urination, swelling of abdomen, hematuria. These symptoms were present in varying severity at different times. For a week the patient had complained of anorexia and vomited for the first time; no convulsions since first attack; no fever; bowels constipated. Urination was scanty and contained blood. W. B. C. 14,000; blood smear negative.

Physical Examination.—General condition good; well nourished.

Glands: Large cervical, axillary and inguinal glands.

Lungs: Slight dulness at left base.

Heart: Right border at right border of sternum, upper border third rib, left border, nipple line. Action regular, sounds good, no murmurs.

Pulse: Regular, no increased tension, good quality.

Liver: Fifth space to free border; just palpable.

Spleen: Ninth rib to anterior axillary line; palpable one finger below costal border.

Abdomen: Lax; tympanitis; left kidney palpable; no general anasarca.

Extremities: Reflexes present; no clonus.

July 22: General condition good, lungs negative, heart borders normal, second sound at base, musical; spleen not palpable; left kidney still palpable.

July 26: Patient was running a slight temperature and passing plenty of urine.

July 30: Lung dulness, diminished voice and breathing at left base persistent. Abdomen slightly distended, some dulness in both flanks, note changing on change of position; urine contained faint trace of albumin, specific gravity low; temperature, respiration and pulse normal.

August 5: Albumin and casts reappeared in the urine.

August 10: General condition about the same. The patient was passing a large amount of urine; 50 ℥ August 9; .9 per cent. urea.

August 22: Passed fair amount of urine.

August 23: Discharged improved.

The temperature during the first three days was 98.8 to 101.6 F.; after that the temperature remained normal. Pulse and respiration were not accelerated. Urine on admission contained albumin, sp. gr. 1,014, acid, many hyaline granular and epithelial casts, red and white blood-cells; 2 per cent. urea.

At discharge the urine was acid, sp. gr. 1,012, contained albumin, a few pus-cells, red blood-cells and epithelial cells.

Treatment.—Tannic acid, Kemp's irrigations, fluid diet; later sodium iodid.

Readmitted, May 8, 1905: Since discharge the patient had been perfectly well; had not complained of headache; no edema of feet at night; no swelling

of abdomen, no nausea or vomiting; passed normal amount of urine; no cardiac palpitation.

Present illness was of one and one-half weeks' duration. During this time the patient complained of headaches and pain in the abdomen; face, feet, legs and abdomen had been swollen and patient had been passing very small quantities of urine; no nausea or vomiting; no fever; bowels moved after cathartic; chief complaint, edema of face and ankles.

Physical Examination.—General condition good; marked puffiness of eyelids; skin and mucous membranes pale.

Lungs: Anteriorly, slight dulness at left apex and in lower part of both axillæ; diminished voice and breathing in lower part of both axillæ; posteriorly, dulness at left apex and on both sides from level of the angle of scapula, merging into flatness at base. Over upper part of dull areas voice and breathing were diminished, first at bases.

Heart: Borders as at last examination; apex beat not distinctly localized; impulse could be felt in fourth and fifth spaces in the nipple line; action slightly irregular; impurity of first sound at apex and accentuation of second sound; accentuated second aortic; no distinct murmurs.

Pulses: Equal, slow, slightly irregular, tension not increased.

Liver: Fourth space, sixth space to just below free border; palpable one finger below free border; not tender.

Spleen: Not felt.

Abdomen: Rounded, generally tympanitic, except for slight dulness in right flank, which does not change with change of position.

Extremities: Cyanosis of feet; marked edema of feet and legs.

May 12: Child was passing very small quantities of urine; edema of lids was more marked; also edema over bridge of nose; edema of legs about the same; well-marked edema of back.

May 14: Edema of face and legs had almost entirely disappeared; still slight edema of tissues of back, and slight dulness at bases.

May 20: Patient was up out of bed and as yet had no recurrence of the edema; difference in weight between when child was edematous and when edema had gone was 8 pounds.

May 29: Discharged improved.

Temperature on admission was 103.6 F. Next morning it was normal and remained so for the remainder of the child's stay at the hospital. Pulse 80 to 100.

Treatment.—Hot baths, salts in the morning; at times nitroglycerin and infusion of digitalis.

Urine on admission, reaction acid, sp. gr. 1,030, albumin positive; many hyaline and granular casts; few red blood-corpuscles and pus corpuscles; at discharge positive for albumin, sp. gr. 1,020, reaction acid; many hyaline casts, few pus corpuscles, bacteria, debris (24-hour specimen). Quantity varied from 9½ ʒ to 36 ʒ in twenty-four hours. The albumin varied from heavy trace to ++.

June 12, 1905, Readmitted.—After discharge for a few days the patient was kept quiet; after that he played rough games in the street. For a week he did not go to school and felt rather weak. Then he was sent to school for three days. For a week there had been edema of lower lids after sleeping. There had been dyspnea on climbing stairs for the last four days; swelling of the feet two or three days, face two days. Bowels moved three or four times a day until this date, when they moved only once. The urine had been steadily diminishing; passed only ʒ iv this date. The child was listless, had no appetite, complained of frontal headache. and the edema was more marked.

Physical Examination.—Edema of face, particularly of eyelids.

Lungs: Dulness with diminished voice and breathing at bases.

Heart: Borders normal; apex beat fourth space just within nipple line; action was arrhythmical, becoming rapid with inspiration and slow at expiration; sounds good; second aortic accentuated; no murmurs.

Pulses: Equal, same arrhythmia as heart; fair quality.

Liver: Fourth space, sixth space to free border; palpable two fingers below free border on deep inspiration.

Spleen: Not felt.

Abdomen: Rounded, rather tense, movable dulness in flanks; fluid wave not obtained; no tenderness; too tense for satisfactory palpation; circumference at level of umbilicus 64 cm.

Extremities: Well marked edema of feet and legs.

June 14: The edema, especially of face, is much more marked than on admission.

June 15: Dr. Lilienthal saw the patient June 14 and considered the case one likely to be benefited by an Edebohls operation.

June 17: Decided improvement in edema.

June 20: The improvement continued and the edema had now almost entirely disappeared; amount of urine in twenty-four hours had increased to over twice as much as on admission.

June 29: General condition about the same; still some puffiness under the eyes and slight edema of back and ankles. For the previous three days the patient had been passing less urine; the previous night had complained of headache. Pulses equal, regular, small, no increased tension. Temperature normal.

Operation.—June 30, decapsulation of kidneys for nephritis by Dr. Elsberg. A 2-inch curved lumbar incision was made and the kidneys exposed. They appeared large and red; capsules easily stripped off; capsules on both sides nonadherent, not tense, so that there was little retraction of the capsule when first incised. Almost the entire capsule on both sides was extirpated; small packing below each kidney; few No. 1 catgut sutures for muscles; silk for skin. Wound healed nicely.

July 1: Edema of back more marked; child passed small amount of urine; puffiness under eyes persisted; edema of lower extremities had increased since the previous night. There was slight edema of the scrotum; circumference of abdomen at level of umbilicus 64 cm.; second aortic sound slightly accentuated; slight increase of pulse tension.

July 6: Theobromin sodium salicylate (diuretin) was started July 5; child passed more urine.

July 7: Was passing small quantities of urine.

July 8: Edema of abdominal wall and flank. Circumference of abdomen at level of umbilicus 69 cm.

July 10: For last three days patient was passing more urine; edema still marked; breath was sweet, pulse good, no increased tension.

July 13: Was passing less urine again; edema less marked; was out of bed.

July 14: Edema of abdomen and scrotum was much less; circumference of abdomen 59 cm.

July 19: Movable dulness in left flank; no edema of scrotum; face was puffy; some edema of back and legs.

August 6: Patient was passing a fair amount of urine, but contains considerable albumin; general condition had improved, and patient was out of bed.

August 12: General condition fair; face was puffy in the morning; slight edema of the legs; heart's action was irregular; passed about ℥xxv of urine a day.

August 14: Discharged improved.

Temperature was normal most of the time; one or two slight rises to 101.4 F.; pulse 80 to 120.

Treatment.—Diuretics, nitroglycerin, warm baths, pilocarpin and saline enemata.

During the patient's stay in the hospital and after operation the urine varied in amount from ℥v to ℥l; sp. gr. 1,010 to 1,034, reaction acid, albumin + to ++; at times boiled solid; urea 105 to 310 gr.; microscopically very many casts, hyaline and granular. The last examination showed it pale in color, acid, sp. gr. 1,016, + for albumin, 0 sugar, 1.27 per cent. urea, 190 gr.; 33 ounces in twenty-four hours. The microscope revealed a few hyalogranular casts and bacteria.

Sept. 10, 1905, the patient was readmitted.

History Since Discharge.—Edema of face and extremities and the enlargement of the abdomen had increased. For about ten days the patient had fever and chilly sensations. For three days the previous week he had severe frontal headache. Slept well, appetite good; had been on a milk diet; bowels had three enemata a day; no vomiting; passed very little urine, which was high colored. The patient was weak, played about the house but not with the boys in the street; heart throbbed very strongly and at times he complained of palpitation. The three principal symptoms were, increasing edema, diminished urine, weakness and headache.

Physical Examination.—General condition good; child pale; slight dilatation of alæ nasi with respiration.

Face: Puffiness, edema of eyelids; edema of back.

Lungs: Anteriorly a few fine crepitant râles over right apex, extending down to third space, and in right axilla to fourth space. Posteriorly lung resonance extended to ninth rib in postaxillary line, on right side (two fingers below angle of scapula). Resonance descended on deep inspiration. On left side resonance extended to seventh space. Resonance descended on deep inspiration. At right apex were a few crepitant and subcrepitant râles. In both interscapular regions inspiration was slightly higher pitched and harsher than normal, and there were a few adventitious sounds. Breathing extended to two fingers below limit of resonance and there were a few subcrepitant râles at left base. Fremitus on right side extended to ninth space; on left side it was obscured by edema.

Heart: Apex beat not visible or palpable. Sounds best heard in fifth space, 8.5 cm. from median line.

R. B. in third space, 2 cm. from median line; in fourth space, 2.5 cm. from median line.

L. B. in third space, 7.25 cm. from median line; in fourth space, 9.25 cm. from median line.

U. B. third rib.

Second sound at apex accentuated and valvular. At base both sounds were accentuated, aortic more than pulmonic.

Pulse: Equal, irregular in force, some increased tension, no thickening.

Liver: Dull fourth space, flat fifth space, to free border; dull tympany one finger below free border; palpable 1½ fingers below free border; edge sharp and firm.

Spleen: Dulness eighth space, flatness ninth space to free border; spleen descended 1½ fingers below free border with deep inspiration; edge firm and rounded.

Abdomen: Lax; diastasis recti; no umbilical hernia; dull tympany in flanks which disappeared with change of position. There was a fluid wave obliterated by very slight median pressure. Circumference at level of imbilicus 63 cm.

Extremities: Moderate edema of legs.

September 11: Hgb. 74 per cent.; W. B. C., 19,800; R. B. C., 4,110,000.

September 13: Edema had increased; patient was not passing sufficient urine.

September 18: Edema was less; passing more urine; movable dulness in left flank; no fluid wave; circumference of abdomen 66 cm.

Edema increased again and then diminished. On November 15 there was no edema of extremities. Pallor was still marked; pulse tension not increased, and no signs of fluid in abdomen.

November 18: Patient had been absolutely free from symptoms referable to general well being for some time.

Temperature was normal most of the time. There were one or two rises. Pulse 70 to 120, respiration 24 to 28.

Treatment.—Hot packs, pilocarpin, fluids, salts.

Urine on admission was amber colored and clear, reaction acid, sp. gr. 1,024, albumin ++, 0 sugar, many hyaline and granular casts. No R. B. C.; few p. c. and epithelial cells; 3 per cent. urea and 129 gr. in twenty-four hours.

The urine improved, there was less albumin and more urea, but this varied; at times the urine was worse. At one time the urine boiled almost solid.

At discharge urine was straw colored, clear, acid, sp. gr. 1,022, albumin, a trace. Microscopically, very few hyalogranular casts; very few p. c. and epithelial cells.

March 31, 1911. The patient remained perfectly well for 4½ years after discharge from the hospital, then was exposed in October and chilled on the roof of school; took off his shoes. He then developed anasarca and for three months was in the hospital and recovered. Had been well since. Was 15 years of age, and weighed 91¼ pounds. He was in fine physical condition, had an excellent color, with no edema, no headaches, or any symptoms; pulse 84 tension, 110 to 120 mm. Hg.; urine sp. gr., 1,015; very few hyaline and granular casts of small caliber; passed 40 to 45 ounces of urine daily; albumin very marked; urea 0.018 to the c.c.; diet mixed; no meat, no eggs, no salt; took soup.

This patient was in the hospital three times suffering from the usual accidents of chronic nephritis. He had been partly relieved each time and discharged and returned with a recrudescence of symptoms. After the operation he improved very slowly, was removed from the hospital, returned and finally recovered completely. He remained well for four and one-half years, and then exposed himself on a roof barefooted in late winter and had a full recrudescence of symptoms. It took three and one-half months for these symptoms to clear up and he was then free from symptoms. He had probably a large kidney with a very large percentage of albumin and some isolated small caliber casts in the urine; urea normal. The patient had absolutely no symptoms. Anyone looking at the boy would think he was in rugged health.

The third case was that of a female child 8 years of age, admitted June 28, 1909, and died Aug. 26, 1909.

There was no history that could be traced as to heredity or exanthemata; she had a self-evident chronic nephritis as shown by operation.

On admission she had been five weeks ill with edema, vomiting and abdominal distention. There were remissions in the intensity of the edema; there were no headaches or convulsions or dyspnea before admission to the hospital. On admission to the service of my assistant (Dr. Henry Heiman) there was general anasarca involving both pleura; not the cardia, and with the hydrothorax there was also ascites. After admission she developed a petechial eruption.

After failure with other forms of treatment and Southey's tubes, convulsions set in a month after her stay in the hospital, and after repeated convulsions she was operated on August 20, fully seven weeks after admission. She never fully rallied from the operation. At the

operation, performed by Dr. Elsberg, the right kidney was shown to be normal in size with an easily stripped capsule, the left to be enlarged and white, bulging through the incision in the capsule. An examination of a piece of the organ showed chronic parenchymatous nephritis.

The urine during the illness was loaded with casts, hyaline and granular, and leukocytes, which were also found after operation. The amount of urine passed in twenty-four hours was not measured.

This case is of great importance as it shows that we cannot rely on the operation to immediately restore the kidney to a power of functionating that is consistent with life, if this has been severely threatened. In all the cases thus far it will be seen that the kidney did not recover itself after operation until the wound had entirely closed, so that it cannot be that the extensive wound itself had anything to do with the relief of the patient, for anasarca did not disappear until the wound had completely closed.

CASE 3.—C. B., female, aged 3 years.

Family History.—Negative.

Previous History.—No scarlet fever, no account of infectious diseases.

Present History.—Five weeks prior to admission, swelling of face, hands, etc.; vomiting a great deal; voiding small quantities. Under a physician's care the edema decreased, then increased. The abdomen became distended.

Physical Examination.—General anasarca; urinous odor to breath.

Lungs: Fluid in both chests; fluid in abdomen.

Von Pirquet test negative.

W. B. C., 26,000; polynuclears, 91 per cent.; leukocytes, 9 per cent.

Urine: Sp. gr. 1,010 to 1,040; albumin, heavy trace to ++; many casts and R. B. C.

Three days after admission a petechial eruption appeared over the abdomen; edema increased in spite of treatment. Southey tubes did not drain well. Necrosis of labia majora developed. Later necrosis spread to other parts of the vulva; erysipelatous eruption also appeared around vulva, which later disappeared.

July 30: Child had convulsions, followed by coma, which cleared up shortly. Urine progressively decreased.

August 11: Paracentesis; 30 c.c. of clear fluid removed.

August 13: Child again in convulsions; temperature rose to 105 F.

August 18: Marked chemosis present; twitching of right forearm present for several days.

August 19: Edebohls' operation performed by Dr. Elsberg. Only left kidney showed "A large white kidney"; right kidney practically normal. After capsules were incised, parenchyma of both kidneys did not bulge and felt soft.

August 20: Since operation the child had not passed any urine, although edema was less marked; pulse good, and of very high tension; face twitched; petechial eruption over both ulnars.

August 21: Temperature subnormal—96 F.—in the morning.

August 23: Low several days; temperature was subnormal, barely rising to normal in the afternoon; at one time temperature was 94.4.

August 25: Child died. Urine did not increase; temperature rose above normal 100.6, and before death to 101 F.

CASE 4.—J. M., male, aged 13.

Family History.—Negative; father 43, well; mother died at 33; cause unknown; four other children alive and well.

Past History.—Infancy normal; measles when 2 years old; diphtheria at 6 years—recognized when child had paralysis of palate following it; remained in Middlesex Hospital, London, for one week, and was discharged cured; no other acute infectious diseases; never before was in a condition like the present.

Present Illness.—Feb. 5, 1910, the child complained of headache, pain in the eyes, and nausea; no vomiting; some chilliness and fever; face became puffy, most marked around the eyes; child had also general discomfort and malaise; also cramps in the abdomen; edema of the feet was noticed February 9; child felt indisposed and had no appetite.

Physical Examination.—Feb. 10, 1910, examined by Dr. Hahn; general condition good; well nourished; marked edema around both eyes; edema about back of scalp.

Eyes: Edema around both eyes, pupils react; edema on back of scalp; movements normal; conjunctiva congested.

Mouth: Teeth and gums in good condition; throat clear; tonsils large; no paralysis of soft palate.

Head and neck: Glands not enlarged.

Chest: Lungs negative.

Skin: Edema of skin general.

Heart: Apex beat, fourth space, nipple line. Borders: Right at right sternal border; upper at second space; left in nipple line; action, regular, slow, forcible; second pulmonic reduplicated; no murmurs; pulse regular, large, slow, of moderate tension.

Liver: Fifth rib to free border; not felt.

Spleen: Not felt.

Abdomen: Somewhat distended, soft, tympanitic; edema of skin on abdominal wall and chest.

Extremities: Reflexes present; edema of both lower extremities; most marked on thighs.

Genitals: Normal.

Rectal: Not made.

Synopsis: Edema.

February 10: Fundi negative.

February 15: Edema increased in scrotum and lower extremities; urine gradually diminishing.

March 1: Patient complained of abdominal pain; edema of face increasing; large amount of edema in the back; signs of large amount of edema in the abdomen.

Lungs: Posteriorly, dulness and diminished breathing on right side beginning two fingers below the angle; on the left side two fingers above the angle.

March 21: General condition good; edema of face diminishing; there was marked edema of the back, abdominal wall, genitals, and lower extremities. There were signs of fluid in both chests beginning at the angle of scapula on right side and one space above angle on the left side; apex beat in fifth space, one finger outside the nipple; heart action regular and slow; second aortic sound accentuated; signs of fluid in the abdomen.

April 15: Patient this morning showed less edema of lower extremities; considerable edema of back and some puffiness of face; passed limited quantity of urine; patient's general condition not much improved after first week after admission; for past two months general anasarca stationary; secretion of urine sometimes increased; sometimes diminished under the most diverse management; no headache; confined to bed since admission.

Temperature, remained normal except on two occasions when it went to 101.4 F.

Operation.—In view of the absolute standstill condition and confinement of patient to bed and utter helplessness, an operation was advised and performed by Dr. Lilienthal, April 18, after a stay of eight weeks in the hospital.

April 18: Bilateral Edebohls performed in usual way, using fourth oblique incision in approaching kidney. Large "white" kidney found.

April 24: Abdominal distention did not show much change; face and legs greatly reduced; superficial dressings changed daily; always soaked with fluid.

April 30: Eyelids puffed.

May 4: Abdominal paracentesis done by Dr. Ryttenberg; 2,500 c.c. slightly turbid, yellowish white fluid removed.

May 13: Considerable edema of back below wounds; edema of face not so marked; temperature normal; wounds granulating.

May 14: Twenty-four-hour specimen of urine gave too much albumin to be measured by the Eschbach method.

May 18: Edema slowly increasing on thighs, scrotum, abdominal wall and back; much fluid in abdomen; slight edema of feet and legs; voided 600 to 700 c.c. a day; urine examination showed little improvement.

Urine Examination: Before operation, sp. gr. 1,010 to 1,020, pale, amber, clear; albumin present; very many hyaline and granular casts; R. B. C.; few W. B. C. Amounts of urine varied between 100 c.c. and 800 c.c. per diem. Amount immediately after operation, 615 c.c.; two days later, 1,500 c.c.; third day, 1,575 c.c.; fourth day, 1,100 c.c.; fifth day, 1,325 c.c.; sixth day, 1,500 c.c. From this time on the amounts diminished. On the twenty-first day the amount was 425 c.c. After that it varied between 600 and 825; on day of discharge it was 1,380 c.c.; albumin still +++; casts were moderate in number; few R. B. C.; many W. B. C.

May 1: Discharged to convalescent home.

Oct. 22, 1910, returned for examination; found in excellent condition, weighing 85 pounds; had been in good health all summer; no symptoms whatever; color good.

Urine: Trace of albumin, no casts. (Urine passed in office.)

Jan. 8, 1911: The patient had remained well; weighed 85½ pounds; urine + for albumin; sp. gr. 1,020; few hyaline and granular casts and leukocytes; arterial pressure 120 to 105.

March 14, 1911: Urine + for albumin; few small caliber casts, hyaline and granular; arterial pressure 120 to 110; weight 91 pounds; color excellent; in perfect health; no headaches.

This is really the most brilliant case of the series because improvement was coincident, within a few days, with the operation. The boy was well taken care of, protected from cold and on a very strict diet after the operation. He had never been in as good a condition of health and this freedom from symptoms continued to a year after operation. In this case also the urine still showed marked disease of the kidney, but the arterial tension was practically normal and there were no circulatory signs.

The fifth case in which operation was done is peculiar in that there was always a slight amount of general edema of the surface and the urine was diminished in amount, the patient confined to bed in a semi-soporous state, with no ambition, and nothing in the form of diuresis was of avail in increasing the amount of urine or in rousing the patient from his invalid state. After operation he improved, then relapsed, and finally permanently improved and remained well, being free from symptoms six months after the operation.

CASE 5.—A. S., male, aged 5 years; in the hospital Oct. 11, 1909, to Jan. 23, 1910.

Family History.—Negative.

Previous History.—Measles at 2 years, no scarlet fever, or other account of infectious diseases.

Present Illness.—Began eight days prior to admission with edema of face and legs, diminished urination, headache.

Physical Examination.—Swelling and edema of face, eyelids, scalp and legs; eyes could not be opened on account of edema of eyelids.

Lungs: Showed fine moist râles in left base and both axillæ, flatness, distant breathing and voice from right of scapula to base.

Abdomen contained no fluid.

Urine: Hyaline and granular casts; trace of albumin; sp. gr. 1,016 to 1,030; acid, amber, clear.

Blood: Hgb. 94 per cent.

For a time edema decreased and urine output increased. Later the original conditions returned. About two weeks before discharge the patient received theobromin sodium salicylate (diuretin) for six days, increasing the urine output from 375 c.c. to 955 c.c.

On discharge the urine showed sp. gr. 1,006, heavy trace of albumin and a few granular casts; edema of body much decreased.

July 28, 1910, readmitted to hospital.

Physical Examination.—Marked edema around eyes; skin covered with small vesicles; edema of extremities; movable dulness in abdomen; fluid on both sides of chest.

August 1: Urine small in amount.

August 4: Prolapsus ani occurred and replaced.

September 5: General condition good; on general diet; edema much diminished; urine still small in amount; responded to hot packs.

September 18: Prolapsus of rectum reduced.

September 23: Fluid in abdomen increasing.

November 1: Urine showed exaggeration of nephritis under full diet and forced fluids.

November 10: In last six days, exacerbation of edema especially around face; urination scanty, 50 to 100 c.c. daily; showed slight evidences of uremia; no evidence of serous effusion anywhere.

Temperature in greater part varied between 98 and 100.2 F., occasionally rising to 104; pulse 100 to 120; respiration 24 to 28.

Blood: 98 mm. Hgb.

Urine, dark amber, clear, acid, sp. gr. 1,024 to 1,038; very heavy trace of albumin; many hyaline and granular casts; few R. B. C. and W. B. C.; this picture varied at times as the condition improved.

Hemoglobin, 65 per cent.

November 13: Operated on by Dr. Lilienthal. Four-inch lumbar incision made for extraperitoneal exposure. Fibrous capsule nicked and stuffed away; gauze packed around kidney. Kidneys showed "Large white kidney" of chronic parenchymatous nephritis. Operation lasted six minutes.

November 21: First dressing; gauze removed; kidneys less swollen.

December 3: For the previous few days the edema had increased; wounds healing.

Summary from day after operation to December 3: Immediately following operation the general condition improved, edema decreased, patient became noticeably brighter. This improvement remained for two weeks, after which edema increased and amount of urine decreased.

URINE EXAMINATION

Date	Amt. c.c.	Date	Amt. c.c.
November—		November—	
13	25	24	515
14	160	25	435
15	115	26	505
16	190	27	525
17	165	28	370
18	220	29	395
19	125	30	225
20	125	December—	
21	150	1	350
22	715	2	200
23	520		

At all times the urine contained a heavy trace of albumin; sp. gr. 1,014 to 1,024; many hyaline and granular casts.

Diet was forced fluids; total ℨl to ℨlxxx per day.

December 11: Under restricted diet and no medication, well marked diuresis was established. Urine amounted to 1,000 c.c. Hgb. 45 per cent.

January 16: General condition good; up and about; full diet; gaining in weight every week; no edema; voiding large quantities of urine.

January 27: Urine still contains casts; general condition good.

January 31: Urine is amber, clear; sp. gr. 1,016; faint trace of albumin and few W. B. C.

March 31, 1911: Four and one-half months after operation; has been out of hospital since January 31; is pale but has absolutely no edema. Weight 46 pounds.

Urine: Albumin very marked; quantity 7 parts *pro mille;* urea 1.8 per cent.; abundant hyaline, granular and epithelial casts.

In reviewing the five cases I wish to emphasize the fact that with the exception of Case 3 all were carefully selected for the procedure of Edebohls after I had failed with a reasonable trial of well-known internal methods. I think there are two facts which stand out quite sharply on the canvas, and these are, first, the absolute well-being of the patients in the successful cases for great lengths of time after operation, and this for greater periods than with medicinal agents in the face of continued signs in the urine of grave disease of the kidney persisting after the operation; and second, that, as in Case 2, the kidney if exposed after operation to exciting agents will give symptoms and still be able to recover itself as if no operation had been performed. In other words, the operation has not compromised the recuperative powers of the kidney.

Improvement does not set in immediately after the operation, as one would be led to believe, but only, it seems, after the surgical wounds have thoroughly healed and the kidney has become accustomed to the new local circulatory conditions. The well-being of the patient is more striking than after recovery from medicinal therapy. It is, as one would be led to believe from a study of Case 3, inadvisable to operate in the face of acute uremic symptoms.

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PROGRESS IN PEDIATRICS

ACUTE INFECTIOUS DISEASES

Epidemic Cerebrospinal Meningitis

A Review of the Recent Literature

The discovery of the diplococcus intracellularis meningitidis by Weichselbaum, in 1887, led to a prolonged controversial discussion as to the organism's specifically for this type of meningitis. Bonomé, Jaeger and Heubner assumed either that more than one organism was concerned in the causation of this disease, or that the *Diplococcus intracellularis* did not show constant morphologic and staining characteristics. The final establishment of the claim of Weichselbaum that this organism is the sole specific agent of epidemic meningitis came recently with the development of bacteriology along the lines of specific reactions, more particularly the precipitin and complement fixation reactions. With the definite settlement of this important point in the etiology of the disease, other problems of great importance came to the fore.

Though meningitis, as shown by the name most commonly employed, has appeared in repeated and very extensive epidemics, the strange and apparently inexplicable phenomenon has often been observed that despite lack of isolation either at home or in public institutions, but few cases have been reported in which direct contagion could be traced. With the development of reliable methods for isolating the meningococcus, numerous studies have appeared on its presence in the nasopharynx of normal individuals coming in intimate contact with patients suffering from the disease.

Von Lingelsheim was one of the first to work along these lines, and his observations have been confirmed by Dopter, Bruns and Hahn, Bochalli, Selters, and others. Albrecht and Ghon have described epidemics of rhinopharyngitis due to the meningococcus, observed during an epidemic of meningitis. These facts and the postmortem findings of marked swelling of the pharyngeal tonsil and posterior part of the nasopharynx by Westentoefer in twenty-nine cases of meningitis, speak strongly for the nasopharyngeal route of infection. Dopter,[1] basing his views on his own observations and on those previously mentioned, denies the existence of such a condition as an epidemic of meningitis. It is more exact to speak of an epidemic of meningococcic rhinopharyngitis in the course of which a certain number of individuals develop meningitis as a complication. What determines the occurrence of this complication, whether it is the virulence of the particular strain of the organism, deficiency of the local or general immunity products in certain individuals, the physiologic or anatomic peculiarities of the vascular and lymphatic apparatus of the nasopharynx, or the seasonal influences, is at the present stage of our knowledge purely hypothetical. Work along this rather neglected field of research is urgently needed. Experimental meningitis has advanced to such a stage that it would seem as though some of these important problems were capable of solution. Moreover, granted that the nasopharynx is the primary portal of entry, we are still in doubt as to the route along which the meningococcus reaches the meninges. While many, Flexner among them, consider the lymphatic route the most probable, anatomic and pathologic studies on the lymphatic circulation of the nasopharynx seem to throw some doubt on this view. Bacteriologic studies of the blood in the very early stages of the disease have not been sufficiently numerous to be helpful in the solution of this problem.

1. Dopter: La Prophylaxie et la Traitement de la Méningite Cérébrospinale Epidémique, Jour. méd. Francais, iii, 106.

The symptomatology of epidemic cerebrospinal meningitis is so well established that little of novelty can be expected in the recent literature. Macgregor[2] in a paper on the immunity phenomena in this form of meningitis, divides the disease into three periods:

First Period: Acute general infection with recovery by crisis, usually within the first week. Associated with this is a marked production of agglutinins proportionate to the severity, duration, and degree of reaction. The opsonic index becomes definitely raised within the first week.

Second Period: There are present symptoms of local irritation, and the toxic phenomena such as emaciation, increased urea excretion and erythrophagocytosis are due to metabolic disturbances. Recovery takes place by lysis, usually within four weeks. The agglutinins in this period diminish, while the opsonins increase or continue high.

Third Period: This is very chronic, with a variable temperature. The exudate is scanty, and the organisms persist in the cerebrospinal fluid. Agglutinins are absent, while the opsonic index remains as in the second period. Macgregor found no opsonins in the cerebrospinal fluid, even when they were abundant in the blood. Repeated removal of the fluid by lumbar puncture did not stimulate the formation of opsonins.

A notable study on the cerebrospinal fluid in the infective diseases of the meninges has recently been contributed by Connal.[3] Among other cases there were 152 of epidemic meningitis in which the character of the cerebrospinal fluid was carefully studied. The highest intracranial pressure was found in the early stages, in which reaccumulation of fluid takes place rapidly. Often it rises above normal within a few hours after a puncture. Increased pressure is a constant phenomenon and often persists for some time after subsidence of the disease. The normal transparency of the fluid is almost always lost, and the degree of turbidity indicates the extent of the exudate. A yellowish or greenish color in a turbid fluid is significant of a virulent infection. Organization or absorption of the exudate is shown by clearing up of the fluid, but as long as exudate is present, some degree of opalescence persists. The presence of a coagulum is one of the earliest signs of meningeal inflammation, and is the last to disappear. The alkalinity is reduced, due to the formation of lactic acid from the dextrose by the meningococcus. In the later stages of the disease, the meningococcus loses the power of converting dextrose into lactic acid, so that the alkalinity once more approaches the normal. The amount of albumin present is a reliable measure of the severity of the inflammatory process. The absence of a reducing sugar is pathognomonic of meningeal inflammation. The reappearance of sugar indicates, in most cases, beginning recovery. The polynuclears show marked increase, depending on the acuteness of the inflammation. Mononuclears predominate at the termination of the disease; these cells may persist for some time after convalescence. The presence of endothelial cells is also indicative of meningeal inflammation, their number being proportional to the severity of the inflammatory process. In acute cases, after the first few days, large numbers are found. The number of endothelial cells increases with extension or aggravation of the morbid process. At the termination of the disease they are seen in large numbers, sometimes cemented together. The presence of a large number of meningococci is an unfavorable sign: persistence of extracellular diplococci is seen in fatal cases. Death, however, may ensue even when all the organisms are within the cells.

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2. Macgregor: Immunity Phenomena in Cerebrospinal Meningitis, Jour. Path. and Bact., xiv, 503.

3. Connal: A Study of the Cerebrospinal Fluid in the Infective Disease of the Meninges with Special Reference to Cerebrospinal Fever, Quart. Jour. Med., iii, 152.

Netter and Debré have observed clear fluid either in the early or late stages of cerebrospinal meningitis, and in abortive cases. Not infrequently they found meningococci in clear fluid. The French observers consider the precipitin reaction of Vincent and Bellot and the fixation reaction of Bordet and Gengou of diagnostic value in the cases in which the meningococcus can not be found in the fluid. Kirchner found an agglutination reaction in the blood in 55.2 per cent. of his patients. It can readily be seen from his observations and those of Macgregor that the examination of the blood can not supplant that of the cerebrospinal fluid in the diagnosis of meningitis.

Salebert and Thurbert[4] describe the constant occurrence of polyuria associated with increased excretion of urinary constituents in patients with cerebrospinal meningitis. Similar observations are recorded by Apert and Griffon, Nattan Larrier, Loeper and Gouraud. The polyuria and the increase in nitrogen, chlorids and phosphates, and the occasional presence of glycosuria are assumed to be due to irritation of the centers in the medulla, and are considered pathognomonic by these French observers.

The therapy of epidemic meningitis was, until recently, one of the most unsatisfactory in the whole field of medicine. Despite all kinds of symptomatic remedies, despite repeated lumbar punctures, so highly lauded at one time, despite intradural lysol injections, subcutaneous injections of diphtheria antitoxin, and the use of vaccines, the enormously high rate of mortality remained unchanged from year to year. With the opportunities for experimental work presented by the recent epidemics in the United States, Germany, and France, the therapy of this disease entered a new phase. Practically simultaneously, Kolle and Wassermann, Jochmann and Flexner prepared antisera which, from their effect on experimental meningitis, justified the hope that a valuable therapeutic agent had at last been discovered. Applied subcutaneously, as was first done in Germany, it was soon found to be of no value in this manner of application. To Flexner belongs the lasting credit of insisting from the first on its intralumbal application. He argued that if the serum is to be effective, it must come in contact with the meningococcus in a concentrated form, and this could be accomplished only by injecting the serum directly in the spinal canal.

The details of the mode of preparation of the serum can not here be given; suffice it to say that Flexner prepares his serum by injecting a horse once a week alternately with dead cultures and autolysate of many strains of the meningococcus. In the course of eight months a sufficiently potent serum is derived.

By a wise mode of distribution, permitting the use of the serum by trained observers only, Flexner soon obtained sufficient data indicating the value of this mode of treatment. In his most recent paper[5] he reports on 712 collective cases, showing a mortality of 31.4 per cent. The appended table from his paper shows the mortality at various age periods:

Age, Years	Cases	Mortality, Per cent.
1-2	104	42.3
2-5	112	26.7
5-10	113	15.9
10-15	101	27.7
15-20	107	32.7
Over 20	175	39.4

According to Dopter[6] 158 patients treated with the Kolle-Wassermann serum by Krohne, Levy, Hahn, Tobben and Grocco, yielded a collective mortality of

4. Salebert and Thurbert: Syndrome Urinaire Paradox Rev. de méd., xxx, 205.

5. Flexner: Antimeningitis Serum and the Results of Its Employment, Internat. Clin., Series 19, iv, 1.

6. Dopter: La Sérothérapie Antiméningococcique, Ann. de l'Inst. Pasteur xxiv, 96.

18.35 per cent. Krohne[7] reports on serum treated patients who came under his observation in the gubernatorial district of Düsseldorf. He injected intraspinally the Kolle-Wassermann serum in twenty-two cases with six deaths, a mortality of 27.3 per cent.

E. Levy[8] employed the Kolle-Wassermann serum given intraspinally in twenty-three cases in the barracks at Essen; there were five deaths, a mortality of 21.74 per cent.

Holm[9] used the same serum and technic at Essen in forty-one cases with five deaths, or a mortality of 12.1 per cent.

Többen[10] treated twenty-nine patients similarly at Bochum with a mortality of 34.5 per cent. In twelve of these cases, in which treatment was begun on the first or second day of the disease, the mortality was only 16.6 per cent.

E. Grocco[11] used the same method and serum at Milan in ten cases, with two deaths, or a mortality of 20 per cent.

Schoene, using the Jochmann serum, obtained a mortality of 27 per cent. Dopter reports on 402 patients treated with a serum prepared by him at the Pasteur Institute, in which the mortality was 16.44 per cent. Excluding seventeen cases injected but a short time before death, two cases in which death was due to other causes, and nineteen other cases excluded for other valid reasons, he derives 383 cases with only forty-seven deaths, a mortality of 12.27 per cent.

A comparative table of mortality at various ages as obtained by Flexner (an earlier report), Netter[12] (Flexner's serum), and Dopter, gives the following instructive data:

Age Years	Flexner, Per cent.	Netter, Per cent.	Dopter, Per cent.
Less than 1	50.0	50.0	48.6
1-2	42.1	0 (6 cases)	20.1
2-5	23.5	16.6	9.3
5-10	11.4	12.5	8.5
10-20	23.8	0 (8 cases)	10.2
Over 20	26.4	0 (8 cases)	14.1

Even more instructive is the table giving the mortality rate with reference to the time of injection:

Time of Injection	Flexner, Per cent.	Netter, Per cent.	Dopter, Per cent.
Before third day	14.9	7.14	8.20
Fourth to seventh day..	22.0	11.1	14.4
After first week	36.4	23.5	24.1

The importance of early injections is here strikingly shown.

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7. Krone: Ueber die bisherigen Erfolge der Behandlung der epidemische Genickstarre mit Genickstarre-Heilserum in Regierungsbezirk Düsseldorf, Ztschr. f. Med., Beamte, Berlin, 1908, xxi.

8. Levy, E.: Erfahrungen mit Kolle-Wassermannschen Meningokokken-Heilserum bei 23 Genickstarrekranken, Klin. Jahrb., Jena, 1907-08, xviii.

9. Holm: Die Ergebnisse der bakteriologischen, cystologischen und chemischen Untersuchung der Lumbalexudate von 37 Genickstarrekranken unter dem einfluss des Kolle-Wassermannschen Meningokokkenserums, Klin. Jahr., Jena., 1908, xx.

10. Többen: Zur Therapie der Meningitis cerebrospinalis epidemica, München. med. Wchnschr., 1907, liv, No. 49.

11. Grocco, E.: Sopra dieci casi di meningite cerebro-spinale epidemica, Gazz. d. osp., Milano, 1909, xxx.

12. Netter: Rareté de Séqueles ches le Sujets guéris de Méningite Cérébro-spinales, à la suite des Injections intrarachidiennes de Sérum antiméningococcique.

Unfortunately, there is at present no unanimity as to the dosage and the details of the serum therapy. Some authorities advise the use of one dose which is to be repeated as often as improvement has become arrested or a relapse has taken place. Dunn[13] has worked out a plan of treatment which those who have not had a large personal experience with the serum would do well to follow. He advises the use of a full dose as soon as cloudy fluid is obtained, without waiting for a bacteriologic examination. The dose should be 30 c.c. if that much can readily be introduced, and as much serum as fluid withdrawn if more than 30 c.c. has been removed. In very severe or fulminating cases, the serum should be reinjected as soon as the patient begins to get worse, or at twelve-hour intervals. In the average case the injection should be repeated daily until four full doses have been given. If the diplococci persist in the fluid after four days' treatment, the injections should be continued until the organisms have disappeared. If subjective symptoms, such as mental impairment or fever, persist after the diplococci have disappeared from the fluid, or after four full doses have been given without progressive improvement, four days should elapse before another course of four daily treatments is begun. When a relapse occurs or meningococci reappear in the fluid, the same treatment should be adopted as for the original attack. In the chronic stage, reappearance of meningococci should lead to the institution of treatment as for an acute attack. In chronic cases with excessive fluid not containing meningococci, daily punctures should be done, but serum should not be injected.

Dunn's[14] figures obtained by following the above outlined method of treatment are very instructive. He compares the mortality at the Boston Children's Hospital previous to 1908 with the results obtained in that year, when serum was first used. Previous to 1908, symptomatic treatment, frequent lumbar punctures, frequent administration of diphtheria antitoxin and vaccines were successively used. The mortality during these years varied from 58 to 80 per cent.; in 1908 on the adoption of serotherapy it fell to 19 per cent.

Sladen[15] in a very thorough and detailed report of the cases (which were all sporadic) at the Johns Hopkins Hospital, shows that there were thirty-three cases up to 1908, with a mortality of 66.6 per cent.; in 1908 there were twenty-three cases with a mortality of 17.4 per cent.

According to Dunn, the effect of the serum is shown most often by a fall in temperature, which is often critical in character. There is rapid improvement in the general condition, consciousness returns, mental dulness disappears. Delirium, headache, hyperesthesia, tenderness of the neck and vomiting are often relieved in twenty-four hours. The rigidity of the neck and Kernig symptom often persist when all other symptoms have disappeared.

Simultaneously with the improvement in the symptoms, the following changes are observed in the cerebrospinal fluid. Within twenty-four hours the diplococci become much less abundant, the majority of the organisms being enclosed in the cells. They show signs of degeneration such as swelling of the protoplasm, feeble staining power, and impaired growth on culture media. After three days there are frequently no meningococci to be found. Not only is the mortality reduced, but the disease is considerably shortened. Moreover, there is a remarkable reduction in the frequency of complications and sequelæ when treatment is begun at an early stage. Flexner reports complications in only 2.56 per cent. of his cases, Netter in 7.5 per cent., and Dopter in 6.2 per cent.

Death is due either to the great severity of the initial infection or to secondary pathologic processes. As concentration is essential to effective action of the serum, the futility of intraspinal injection, when the process is chiefly localized

13. Dunn: The Serum Treatment of Epidemic Cerebrospinal Meningitis, Jour. South Carolina Med. Assn., x, 315.

14. Dunn: Cerebrospinal meningitis, Am. Jour. Dis. Child., 1911, i, 95.

15. Sladen: Epidemic Meningitis and Serum Therapy at Johns Hopkins Hosp., Johns Hopkins Hosp. Rep., xv, 397.

in the brain, can readily be seen. In these cases, it has been proposed to inject serum directly into the ventricles, either through the fontanelle, or, in older children, through a trephine hole. Several successful cases are reported in the literature. When local complications occur, such as arthritis, serum should be injected locally (as was done successfully by Ladd).

The mode of action of the serum is assumed by Flexner[5] to be chiefly bactericidal. It injures the meningococci in such a way as to limit their multiplication and cause rapid disintegration and death. Phagocytosis is greatly increased by the serum. The phagocytes not only destroy the organisms, but also exert a neutralizing effect on the endotoxin, thus preventing injury to the body by too rapid liberation of endotoxin.

The residuum of mortality even with the most skillful use of the serum is still so considerable that unremitting search for efficient prophylactic measures is far from dispensable. The frequency and persistence of meningococcus in the nasopharynx of healthy individuals shows that this will prove to be a task of considerable difficulty. Schubert, according to Selter,[16] found 391 meningococci carriers among 2,025 school children. Various observers have found meningococci in the throat for periods ranging from one week to several months, and the father of one of Selter's patients showed the meningococci in the nasopharynx for at least seven months. Though v. Lingelsheim found that the meningococci usually disappear within fifteen days, there are cases in which they persist indefinitely. These facts clearly indicate that isolation of these "carriers," except under exceptional circumstances, is impracticable. Unfortunately, up to the present time, most of the measures advised and used with the aim of rapidly destroying the meningococcus in the throat, such as insufflation of dried antimeningococcus serum, the use of pyocyanase, and the various local antiseptics, are devoid of effect.

Recently, Vincent and Bellot have advised the adoption of the following plan of treatment. Daily painting of the tonsils and pharynx with iodin in glycerin, 1 to 30, frequent gargling with hydrogen peroxid to 1 to 10, and inhalation four or five times a day of the following mixture:

Iodin	20.0
Guaiacol	2.0
Thymic acid	0.25
Alcohol (60 per cent.)	20.0

With this mode of treatment, Schneider[17] found that there was no growth after four days. Other French observers also recommend this mode of treatment.

Numerous as are the gaps in our present knowledge of cerebrospinal meningitis, the important contributions of the last decade, in which America has played a decidedly gratifying part, justify the hope of an early conquest of this dread disease.

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TUBERCULOSIS AND SYPHILIS

Boston's Hospital School for Tuberculous Children

(*Edwin A. Locke and Timothy J. Murphy: Boston Med. and Surg. Jour., Aug. 17, 1911*)

In July, 1908, the Boston Association for the Relief and Control of Tuberculosis opened a day camp for tuberculous children. The children were kept in

16. Selter: Verhandl. d. Gesellsch. deutsch. Naturforsch. u. Aerzt., 1909, Part 2, No. 2, 577.

17. Schneider: Prophylaxie de la Méningité Cérébrospinale Epidemique et désinfection du Rhinopharynx, Bull. et mém. Soc. méd. d. hop. de Paris, xxix, 192.

the open air for the entire day, and were always under a definite program, including the care of gardens, housework, play, rest, talks on health, and Nature studies. Later, the day camp was changed to an outdoor school and installed in the refectory building in Franklin park. The roofgarden was equipped with canvas curtains, to be used in case of storm or high winds, desks, chairs, etc., and converted into a schoolroom. Here the children remained during the day throughout the entire winter in spite of the hardest storms and coldest weather. All teachers were furnished by the School Department, and held to the same requirements regarding general work as in the ordinary public schools. The children, however, were regarded strictly as sick children, and their entire life in the school regulated in accordance with orders of the visiting physician.

At entrance, each child was assigned a number and provided with a reclining chair, blankets, thick overcoat, paraffined canvas bag with a detachable blanket lining in which to sit or recline, woolen cap, mittens, overshoes, individual drinking-cup and toothbrush; all of which were numbered. By arrangement with the school nurses, all debilitated, anemic or undeveloped children were singled out, examined by the school physicians, and all positive or suspected cases referred by them to the Out-Patient Department for diagnosis. Many children from tuberculous families were also sent for examination by the nurses of the department. Other agencies have cooperated in making this dispensary the center for this special work. In consequence, the children admitted to the Hospital School were referred from this source, although a few were accepted on the recommendation of their family physician. The school was kept open on Saturdays and holidays, experience having demonstrated the bad results of repeated regular absence from the routine of treatment.

By special arrangement, all specimens of sputum and throat culture were examined in the city laboratory. A specimen of sputum from every child, so far as it could be obtained, was sent to the laboratory, and if negative, the examination repeated at weekly intervals. In all, sputum was obtained from but thirty-eight children; tubercle bacilli were found in nine. A culture was made as a routine of all cases of sore throat, and the child isolated at home under the care of the visiting nurses until the report of the examination was known. Likewise, all cases in any way suspicious of the acute exanthemata were sent home and kept under observation until the condition could be safely regarded as non-contagious. In spite of the fact that during the course of the last year several cases of contagious diseases appeared among the children, these rules were so carefully carried out that no case of contagion occurred. The nurse was furnished with written instructions covering all possible emergencies. One of the visiting physicians was always on telephone call, and every medical question of importance referred to him. Three physicians were regularly in attendance, as a rule at least four visits each week being made. Once each month every child was given a complete physical examination. The daily observations regarding the condition of the children were left to the nurse. Those children needing examination of the nose, throat or ears were referred to the Out-Patient Department. Other special conditions were treated in special clinics. Every effort was made to investigate the homes and to improve the conditions so far as possible when unfavorable.

The entire staff of the institution comprised three physicians, a nurse, social worker, dietitian, five teachers, a cook, two maids and a janitor. The Hospital School was in the strictest sense a hospital, organized and administered as such. It was not maintained for the "debilitated" or "anemic" child, but for the tuberculous only. At entrance the physical condition of the child was determined by one of the visiting physicians, and depending on this, he was placed in one of three groups. The daily program for each of these groups was arranged with reference to the amount and nature of the study, exercise and work. Those in Group I were required to follow the regular routine of the school, which included a systematic assignment of work, exercise and study. In Group III no work and a minimum of study and exercise was permitted. Group II was intermediate. Individual exceptions were, of course, frequently made. Absolute rest in the

case of those with active tuberculosis was less rigidly enforced than would be considered wise in the treatment of adults.

Work of various kinds under supervision was arranged and graded so far as possible to suit the ages and fitness of children to perform it. In small groups the available children were assigned for each week to a schedule of duties. These consisted in setting and clearing the tables, washing dishes, sterilizing the eating utensils, dusting, assisting the nurse, watering the flowers, and other such occupations. On their arrival, at 8:15 a. m., the children first washed their hands and prepared for breakfast, which was served at 8:30. At 9, all the children were required to go to the wash room to brush their teeth. Those not assigned to work then went to the open-air room on the roof, where they were given breathing exercises and school work according to their condition. A few of the sicker patients remained in their steamer chairs for the greater part of the time. During the cold weather the school routine was frequently interrupted by short periods of light exercise. From 11:30 to 12, games were allowed. At noon school work ceased and the children prepared the roof for the rest hour. They then filed to the wash room to prepare for dinner at 12:30. Following dinner, the teeth were brushed and all basins and other utensils used in the wash room packed in the sterilizers. By 1:30 they were again in their places on the roof, where they rested in steamer chairs until 3. In the winter the children were kept warm during this period of rest by sleeping bags and blankets. At the close of the rest period exercises, singing, talks by nurses or teachers, and similar exercises occupied the time until 3:30, when the temperatures were taken and the chairs put away. By 4, they had again finished with the same preparations for the table, and sat down to supper. Beginning at 4:30, they were dismissed in small groups, a teacher accompanying them as far as the Dudley Street Transfer Station. On Saturdays and holidays, and during the summer, the teachers not being present, the work of the school was considerably changed. Volunteer workers took them for walks, supervised them in games, gave them talks on Nature or hygiene topics.

The children were not allowed to use ordinary handkerchiefs while at school, but were furnished with paper napkins instead, which, after being used, were placed in paper bags and at the end of each day burned in the furnace.

The closest attention was given to the question of nutrition. At intervals the children brought lists of the food eaten at home for a period of several days, and in the diet prescribed every effort was made to supplement this diet in such a way as to provide a total suited to the particular needs of the individual child. So far as possible, the food served was of the kind which can be provided by the families of the class from which the patients were drawn. A minimum cost was also a determining factor in its selection. This department was entirely in the hands of an expert dietitian, who devoted her entire time to the work. Throughout the year experiments were carried out on selected groups of children to determine the diet best adapted to their needs.

The following menu, calculated with reference to the calories furnished, is an illustration of the average diet.

Breakfast: Cocoa, graham gems and butter, stewed prunes.

Luncheon: Baked beans and brown bread, milk, apple or orange.

Supper: Milk, bread with jelly.

During the first ten months of the year 1910, with an average attendance of 64.25, the average cost of raw food materials per child per day was thirteen and one-fifth cents.

One of the most important features of the work in the Hospital School was the system of bathing carried out. Each child was supplied with an individual basin, soap, toothbrush, mug and comb, all of which, as in the case of the blankets and other articles mentioned above, were marked with the registration number. For the proper care of these the patients were held strictly responsible. Once each week, with few exceptions, every member of the group of children was

required to take a shower bath, the teachers usually assisting the nurse in the work of supervision. Paper napkins were used in the place of hand towels, and tooth picks for nail cleaners. After being used both were burned in the furnaces.

The first cost of equipment was as follows:

Blankets, clothing, etc.	$1,208.21
Household, kitchen and dining-room supplies, hardware and equipment	1,065.51
Furniture and furnishings	357.75
Repairs	158.97
Electric fixtures	50.33
Plumbing	43.96
Medical equipment	14.66
Total capital expenses for school	$2,899.39

For the year 1910-11 the total general operating expenses were $8,231.60, or a cost per patient, per day, of 56 cents. This is exclusive of the School proportion of the general hospital administrative expenses, estimated as $1,277.34, which if added brings the per capita cost per day to 65 cents.

The general results of treatment have, on the whole, been extraordinarily satisfactory. From Oct. 12, 1909, when the Hospital School was taken over by the Boston Consumptives' Hospital, until its close, Jan. 31, 1911, a total of 191 children, ninety-four boys and ninety-seven girls, were treated. One hundred and seventy-four of these were treated during the year ending January, 1911. The patients classed as Stage 1 comprise 66 per cent., those as Stage 2, 24 per cent., and those as Stage 3, 6 per cent. of the total.

Tabulation of the 184 cases, comprising those actually tuberculous, according to the results of treatment shows the following:

	Arrested	Improved	Unimproved	Unknown	Non-tuberculous	Totals
Stage 1	51	53	8	11	4	127
Stage 2	13	23	7	1	1	45
Stage 3	0	6	5	1	0	12
Totals	64	82	20	13	5	184

The "unimproved" were chiefly of two groups: First, those who were too sick to be at the school, having been admitted because no place in a hospital could be provided for them; and second, those who attended for only a short period or very irregularly. The closing of the school further made it necessary to discharge all patients, irrespective of their conditions. About one hundred were registered at the school just before its closing. FRED C. ZAPFFE.

METABOLISM AND NUTRITION

Indicanuria in the New-Born

(A. v. Reuss: Ztschr. f. Kinderh., 1911, iii, Part 1, p. 12)

Von Reuss, working in Schauta's clinic, examined, for indican, 400 specimens of urine from breast-fed children without discoverable abnormality, especially with no infections or intestinal disturbances, in the first nine days of life, with the result that he found indican in from 14 to 42 per cent. of cases, none being found on the first or ninth days, and the largest proportion, 42.1 per cent., on the fourth day. He sums up his conclusions as follows:

Indican is quite frequently found in the urine of breast-fed children in the first week of life, sometimes in notable amount, without the presence of any pathologic conditions that are clinically observable.

It is found in children in good condition, as well as in those failing to increase in weight, in those having frequent evacuations of the bowels as well as in those having a tendency to constipation, and in those taking a scanty amount of food as well as those taking food abundantly.

The indicanuria, as a rule, is lacking on the first day, rare on the second, and is most frequently and abundantaly found on the third and fourth days; but it is not a rare occurrence during the following days.

Two possibilities must be considered with reference to the cause of this indicanuria. Although the meconium and the stool from breast milk show no signs of putrefaction in the intestine, still the occurrence of putrefactive bacteria makes it possible that there is a formation of indol from the intestinal secretion as the cause of the indicanuria. On the other hand, if the assumption of a parenteral origin of the urinary indican is admitted, the indicanuria of new-born children may be taken as an evidence of tissue destruction and may be brought into relation with the other well-known symptoms of such a process. Possibly also the increase of uric acid in the organism of new-born children plays a rôle in the production of indicanuria. These questions need further elucidation.

ACUTE INFECTIOUS DISEASES

Streptococci in Scarlet Fever

(Felix Schleissner: Ztschr. f. Kinderh., 1911, iii, Part 1, p. 28)

Schleissner, working in the pediatric clinic of the Franz Josef Children's Hospital and in the serologic department of the Hygienic Institute of the German University at Prague, reviews the relations of streptococci to scarlet fever, and shows that it has been proved that streptococci are present very abundantly in the throats of scarlet fever patients, and also in a large number of cases in the blood. He discusses the question as to whether they are related in an etiologic way to the disease itself or whether they are to be regarded as an evidence of mixed infection. The methods by which it has been attempted to prove an etiologic relationship are discussed. Three principal methods have been relied on—the power of the blood serum to agglutinate streptococci, the complement-binding principle, and the bactericidal power of the leukocytes. These methods have been used to show that there is a difference between the streptococci found in the blood in scarlet fever and the ordinary streptococci which produce septic manifestations.

In order to arrive at an opinion as to whether the presence of streptococci in the blood indicates a mixed infection, the author examined the histories of cases in which a bacteriologic examination of the blood had been made, with a view to determining whether there was any relation between the course of the fever and the presence of streptococci in the blood. He reasoned that if the presence of streptococci indicated a mixed infection, those cases in which the streptococci were not present would run a milder course than those in which the streptococci were found. The result of this investigation, however, was negative. Schleissner sums up the results of his investigations as follows:

In the investigation of 108 cases of clinical scarlet fever streptococci were found in the blood during life sixty times, or 55 per cent. Of these streptococcic cases, 31 per cent. of the patients had complications, and of those patients free from streptococci, 35 per cent., no connection of the complications with the presence of the streptococci in the blood could be shown.

While formerly by means of bacteriologic methods (agglutination, complement-binding and bactericidal principles) numerous differences between the strep-

tococci of scarlet fever and of sepsis have been noted, it has now also been possible to show that in the blood-serum of patients affected with sepsis immune bodies active against the scarlet fever streptococci were not present, while in the serum of scarlet fever patients they were constantly found. From this the assumption of an essential difference between scarlet fever streptococci and septic streptococci becomes still more probable.

In the scales from various stages of desquamation streptococci could not be demonstrated with certainty microscopically nor by means of cultures. By a comparative examination of the temperature charts of scarlet fever patients it appears that the connection between the course of the fever and the presence of streptococci does not exist.

To set aside the etiologic importance of streptococci and to assign to them a really secondary rôle appears from these experiments not warranted at present.

The facts so far presented are insufficient to furnish exact proof of the etiologic connection of streptococci with scarlet fever.

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The annual meeting of the American Association for the Study and Prevention of Infant Mortality is to be held at Chicago, Nov. 16-18, 1911. The work of the Association will be transacted partly in small sections devoted to special work and partly in larger meetings of a popular nature.

There will be reports on infant welfare work in this country and abroad by Professor C. R. Henderson of Chicago, Dr. Hastings H. Hart, Director Department of Child Helping, Russell Sage Foundation, Assistant Surgeon General J. W. Kerr, U. S. Public Health and Marine-Hospital Service, and others.

The sections with their chairmen are as follows:

City Milk Supply, Prof. E. O. Jordan, University of Chicago.

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